Genitourinary System

(UROLOGIC DISORDERS)

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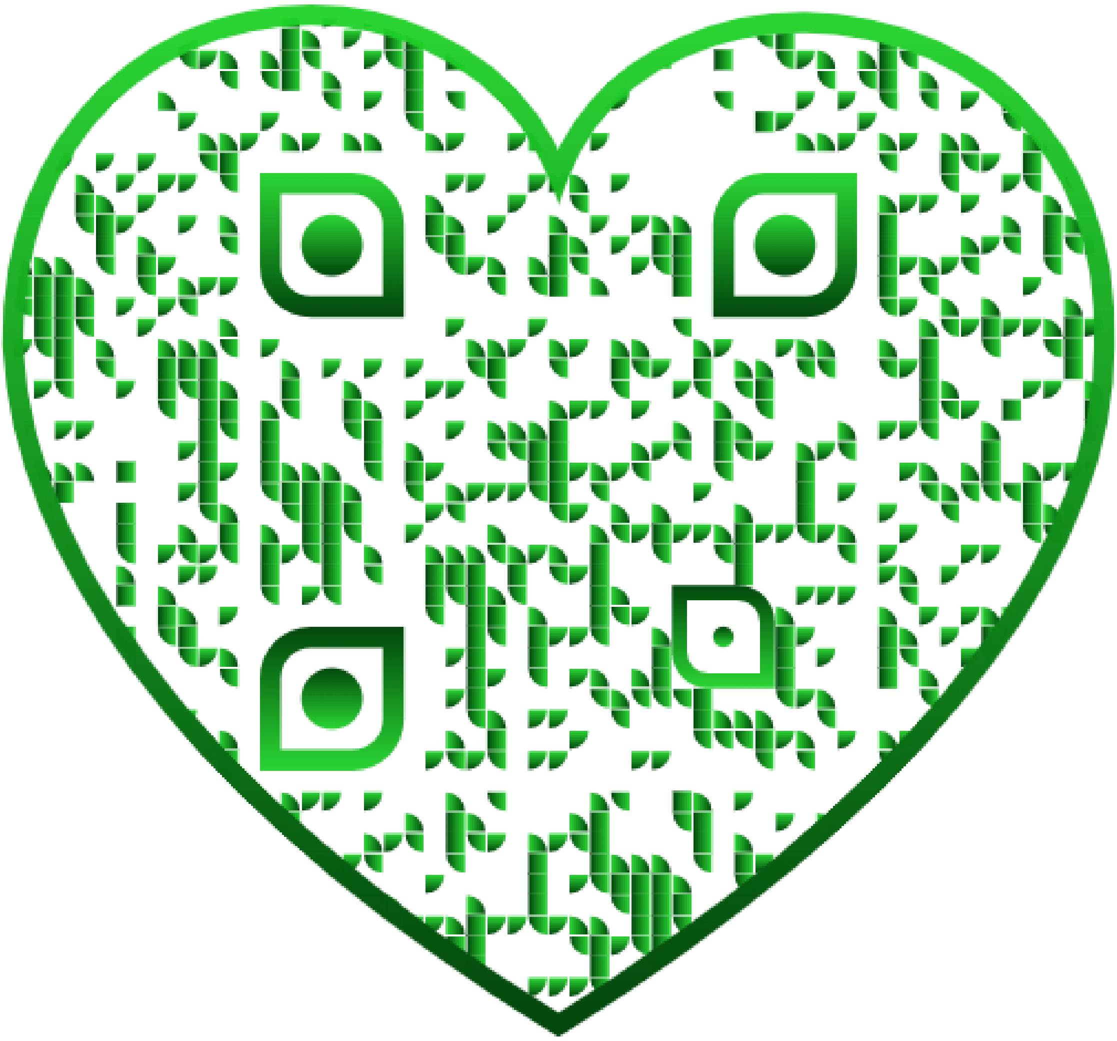
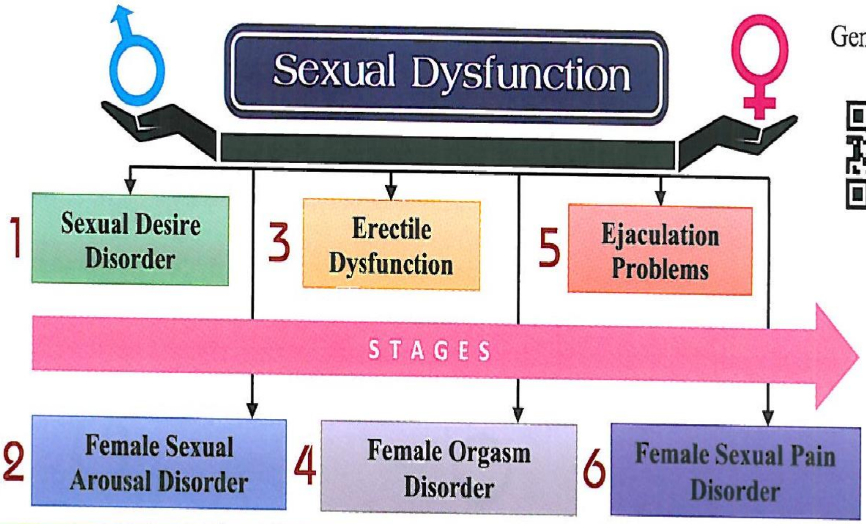
Kidney diseases are separated in special chapter with liver diseases

Urinary Tract Infections (UTIs) are discussed in infectious diseases in chemotherapy chapter





- **Sexual Dysfunction**; is ***difficulty*** *experienced by* an **individual** or a **couple** *during* ***any*** **stage** of a ***normal*** **sexual activity**, including; **libido** (Desire), **arousal**, **erection**, **orgasm** or **ejaculation**.
- **Sexual Dysfunction** ***require*** a ***minimum*** **duration** of *approximately* **6 months**.
- **Sexual Dysfunction** is ***more prevalent*** for **women** (43%) than **men** (31%); 1999 NHSLS

➢ Introduction:-

- **Sexuality**; is a ***complex*** of **multiple factors**; *including* **anatomical**, **physiological**, **psychological**, **developmental**, **cultural** and **relational**.
  - **Sexuality** in **adults** *consists of* ***7 components***;
    1) **Gender identity**; personal conception of oneself as male or female (or rarely; both or neither).
    2) **Orientation**; heterosexuality (attracted to opposite sex), homosexuality (attracted to one's own sex) and bisexuality (attracted to either sex).
    3) **Intention**; what a person actually wants to do with his or her sexual partner.
    4) **Desire (Libido)**; driving force that makes think about sex.
    5) **Arousal**; physiological responses occur in the body and mind as preparation for sexual activity.
    6) **Orgasm**; sudden discharge of accumulated sexual excitement.
    7) **Sexual satisfaction**; feel of relaxing and sexual pleasure in last orgasms.

    Gender identity, orientation, and intention form **sexual identity**, whereas desire, arousal, and orgasm are components of **sexual function**

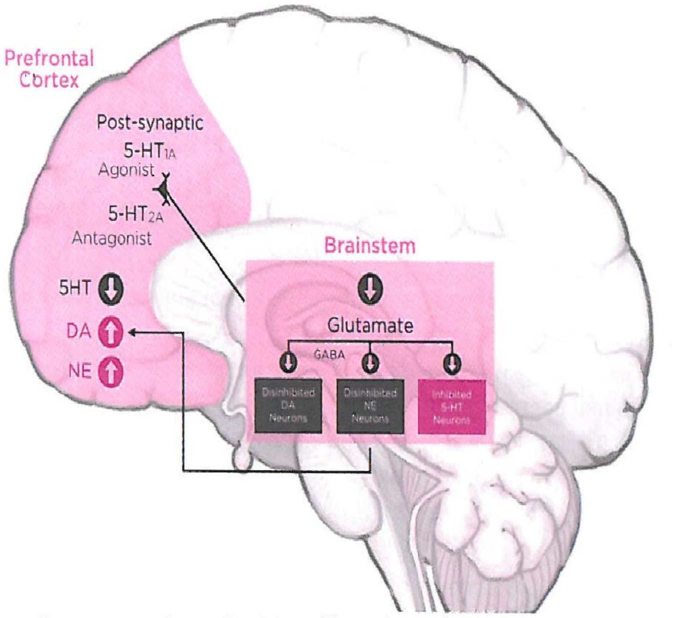
- **Human Sexual Response Cycle**;
  1) **Excitement (Desire) phase**; ***increased***; **heart rate**, **breathing rate**, and **blood pressure** and **flushing (sex flush)**
     - ***In male***;
       - **Erection**; Penis becomes partially erect and full erect after few seconds.
       - **Testicles**; drawn upward toward.
     - ***In female***;
       - **Vasocongestion**; Swelling of the woman's clitoris, labia minora and vagina.
       - **Vagina**; muscle relaxation and produce lubricating liquid.
       - **Nipples**; become hardened and erect.
  2) **Plateau (Arousal) phase**; **period** *between* ***sexual excitement*** *to* **orgasm**.
     - ***In male***;
       - **Urethral sphincter**; contraction (to prevent urine from mixing with semen, and to guard against retrograde ejaculation).
       - **Pre-ejaculatory fluid**; clear, colorless, viscous fluid that is emitted from the urethra of the penis during sexual arousal.
       - **Testicles**; rise closer to the body.
     - ***In female***;
       - **Clitoris**; extremely sensitive.
       - **Vagina**; produce further lubricating liquid.

Female Viagra (Pink Pill)

Flibanserin (Addyi®)

Do not disturb

- **Flibanserin** [flib-AN-ser-in] is the ***first medication* approved** (August, 2015) for the ***treatment*** of **Hypoactive Sexual Desire Disorder (HSDD)** in ***pre-menopausal* women**.
- **Flibanserin** was ***originally*** *developed as* an ***antidepressant***, ***before*** being **using** for **HSDD**.
- **Flibanserin** is *classified as* a ***multifunctional serotonin agonist antagonist*** (**MSAA**).
- *Mechanism of action*;
  - **Flibanserin** ***helps restore*** **rebalancing** of **neurotransmitters** that ***influence*** **sexual desire**.
  - **Flibanserin** ***act as*** **5-HT$_{1A}$** ***agonist*** and **5-HT$_{2A}$** ***antagonist*** → ***increases*** **Dopamine** and **Norepinephrine** (both responsible for sexual excitement) and ***decreasing*** **Serotonin** (responsible for sexual inhibition).


Prefrontal Cortex
Post-synaptic
5-HT1A Agonist
5-HT2A Antagonist
5HT
DA
NE
Brainstem
Glutamate
GABA
Disinhibited DA Neurons
Disinhibited NE Neurons
Inhibited 5-HT Neurons

- *Dose*; **100 mg orally once** *per* **day** at **bedtime** (discontinue after 8 weeks if no response).
- *Most common side effects*; **dizziness, nausea, fatigue, sedation** or **insomnia** and **hypotension**.
- **FDA** *warning*;
  - **Flibanserin** and **Alcohol** ***intake increases*** the **risk** of ***severe*** **hypotension** and **syncope**.
  - ***Contraindicated*** with *strong* or *moderate* **CYP3A4 Inhibitors**.
  - ***Contraindicated*** in *patients with* **hepatic impairment**.

Others (off-label)

Amphetamine (Adderall®) | Methylphenidate (Ritalin®)

- **Amphetamine** and **Methylphenidate** can ***increase*** **sexual desire** by ***increasing*** **Dopamine release**.

Bupropion (Wellbutrin®)

- **Bupropion** is a **norepinephrine-dopamine** ***reuptake*** **inhibitor (NDRI)**.
- **Bupropion** is the ***drug of choice*** for the **treatment** of **SSRI-induced sexual dysfunction**.
- **Bupropion** can ***increase*** **libido** in **women** who are ***not depressed***.

Ginseng | *Ginkgo biloba* | Yohimbine

- **Herbal supplements**, such as **Yohimbine**, ***Ginkgo biloba*** and **Ginseng**, are purported to ***increase*** **desire**, in both **men** and **women**, but this has ***not been*** **confirmed** in **studies**.

Other (*under development*)

Bremelanotide or PT-141

- **Bremelanotide** or **PT-141**; is a ***peptide drug*** which has been ***under development*** by **Palatin Technologies** as a ***treatment*** for **Female Sexual Dysfunction (FSD)**.
- **Bremelanotide** also ***effective*** in treating **sexual dysfunction** in ***both*** **men (erectile dysfunction** or **impotence)** and **women (sexual desire disorder** and **sexual arousal disorder)**.
- ***Unlike*** **Sildenafil**, it ***does not*** act by **vasodilatation**, but ***directly*** **increases sexual desire** and **arousal** via ***acting*** in the **brain**.
- *Mechanism*; ***non-selective*** **agonist** of ***all*** of the **Melanocortin** ***receptors*** *except* MC_2.
- *Uses* (***not*** **approved**);
  - **Hypoactive Sexual Desire Disorder (HSDD)**.
  - **Female Sexual Arousal Disorder (FSAD)**.
  - ***Mixed*** **FSAD/HSDD**.
- **Bremelanotide** was *originally tested* for **intranasal** *administration*, but this application was temporarily discontinued in 2008 after ***increased*** **blood pressure**.
- In 2014, **Bremelanotide** was used in clinical trials as a **subcutaneous drug delivery system** that appears to have ***little effect*** on **blood pressure**.
- The company is expected to seek approval of **Bremelanotide** for this indication in the US in the second half of 2017.

Tibolone (Livial®)

- **Tibolone** is a ***synthetic steroid*** with ***selective tissue estrogenic activity regulator*** **(STEAR)**; with ***desirable*** **effects** in **bone**, **brain** and **vagina** (***not approved*** **in US FDA**).
- **Tibolone** *used as* ***hormone replacement therapy*** in **post-menopausal women**.
- **Tibolone** has also been *investigated as* a ***possible*** **treatment** for **Female Sexual Dysfunction (FSD)** in **Hypoactive Sexual Desire Disorder (HSDD)**.

2) Female Sexual Arousal Disorder (FSAD)

Not be confused with a **Sexual Desire Disorder**

The term **Female Sexual Arousal Disorder (FSAD)** is *often used* in **women**,
while the term **Erectile Dysfunction (ED)** is *often used* for **men**.

➢ Overview:-

- **Arousal**; a ***number of changes*** in the **body** and **mind** *during* **sexual activity**.
  - ***In male***; **Vasodilation**
    - **Penis**; Erection.
    - **Testicles**; scrotum is pulled and testicles rise closer to the body.
    - **Urethral sphincter**; contraction.
    - **Pre-ejaculatory fluid**; clear, colorless, viscous (*not* semen).
    - **Other changes**; ***increased***; **heart rate**, **breathing rate**, and **blood pressure** and **flushing (sex flush)**.
  - ***In female***; **Vasodilation**
    - **Vasocongestion**; Swelling of the woman's clitoris, labia minora and vagina.
    - **Vagina**; muscle relaxation and produce lubricating liquid.
    - **Nipples**; become hardened and erect.
    - **Other changes**; ***increased***; **heart rate**, **breathing rate**, and **blood pressure** and **flushing (sex flush)**.
- **Female Sexual Arousal Disorder (FSAD)**; ***inability*** to **complete sexual activity** with ***adequate*** **lubrication**.

➢ Prevalence:-

- **6-28%** of **women**, that **prevalence** ***increases*** with ***increasing*** **age**.
- **FSAD** ***often affects*** **women** with **gynecologic** or **chronic medical conditions** and those who are taking **certain medications** (*especially* **SSRIs**).

- **Symptoms:-**
  - *Lack* of vaginal lubrication.
  - *Lack* of vaginal dilation or lengthening.
  - *Decreased* genital tumescence or swelling.
  - *Decreased* genital or nipple sensation.
- **DSM-5 Diagnostic Criteria:-**
  - At ***minimum*** **3 of the following** for ***at least*** **6 months**;
    1) *Little* **interest** in **sex**.
    2) *Few* **thoughts related** *to* **sex**.
    3) *Decreased* **start** and **rejecting** of **sex**.
    4) *Little* **pleasure** *during* **sex** ***most*** of the **time**.
    5) *Decreased* **interest** in **sex** *even* when ***exposed*** to **erotic stimuli**.
    6) *Little* **genital sensations** *during* **sex** ***most*** of the **time**.
- **Factors Affect Arousal:-**
  - **Individual factors**; **stress**, **fatigue**, **gender identity**, **health**, **wrong sexual beliefs** and ***over* exposure** to **pornography** is also thought to *lead to* ***poor*** **body image**, **self-consciousness** and *lowered* **self-esteem**.
  - **Hormonal**; *low level* of **Estrogen** and *age-related* ***decrease*** in **Testosterone**.
  - **Physical factors**; **Postmenopausal** (atrophic vaginitis), **vaginitis** (*infection*) and **diabetes**.
  - **Physiological factors**; ***not so clear***.
  - **Medications**; **SSRIs** *can cause* **FSAD** and may *become* **permanent**.
- **Treatments:-**
  - **Psychotherapy**.
  - **Pharmacotherapy**;

Hormone Replacement Therapy

Estrogen

- **Local Estrogen therapy** in **postmenopausal women** can ***improve*** **clitoral** and **vaginal sensitivity**, ***increase*** **libido** and **arousal**, ***decrease*** **vaginal dryness** and **pain** *during* **intercourse**.

Vasodilator

Sildenafil (Viagra®)

- ***Topical*** **phosphodiesterase inhibitors** such as **Sildenafil** have been shown to have ***limited benefit*** in **women** with **sexual arousal disorder**.

Alprostadil (Caverject®)

- **Alprostadil** [al-PROS-ta-dil] is a **prostaglandin** E_1 (PGE_1) ***analogue*** used in **male erectile dysfunction** as an **intracavernous** ***injection*** or **urethral** ***suppository***.
- ***Topical*** **Alprostadil** has been shown to ***increase*** **blood flow** to the **vaginal area** by **vasodilation** and *shows efficacy* in **Female Sexual Arousal Disorder** (***off-label***).
- ***Adverse reactions***; **vaginal burning** and **irritation**.

Other (under development)

Apomorphine

- **Apomorphine** is a ***dopamine agonists*** that are ***approved for*** the ***treatment of*** **Parkinson's disease**.
- ***Sublingual*** **Apomorphine** (2-3 mg) *thought to* ***enhance*** **sexual response** *due to* **stimuli** in **FSAD**.

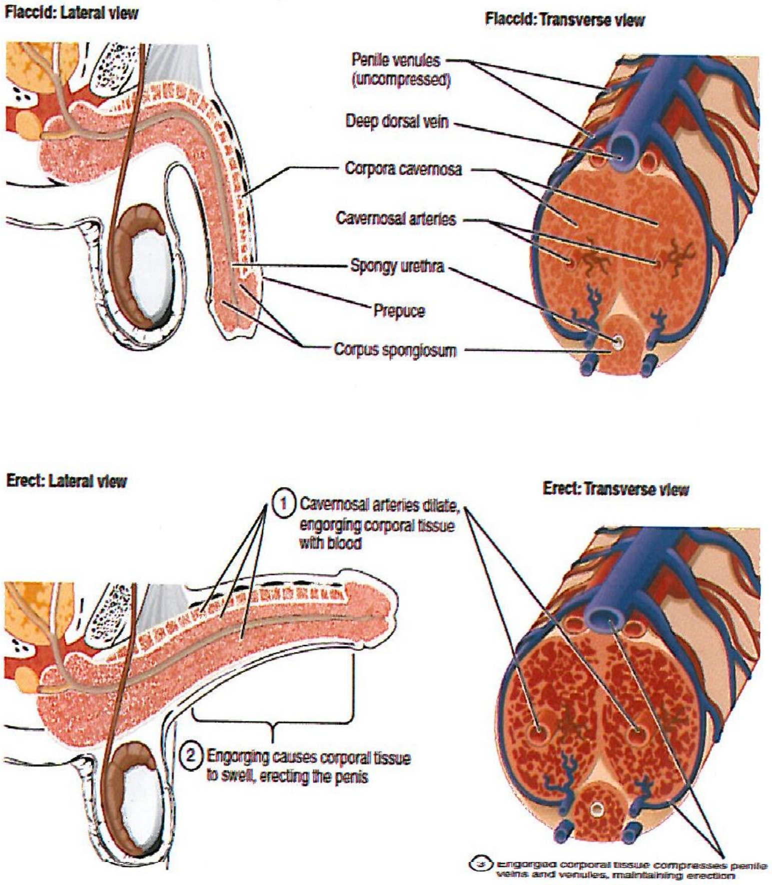
Bremelanotide or PT-141

- **Bremelanotide** is *effective* in **Female Sexual Arousal Disorder**; *see previous page*.

  - **Device Therapy**; ***vacuum devices*** such as **EROS-CTD**
    - **EROS-CTD device** is *designed to* ***treat*** **Female Sexual Arousal Disorder** and is ***approved for*** **women** who *experience* ***reduced*** **sensation**, **lubrication**, and *ability to achieve* **orgasm**.
    - The **device** ***consists of*** a ***small*** **vacuum pump** that is ***placed over*** the **clitoris** to ***apply*** **gentle suction** to the **region** and ***increase*** **blood flow**, ***aiding*** in **sexual arousal**.

3) Erectile Dysfunction (ED)

- **Definition:-**
  - **Erectile dysfunction** (**ED**) or **Impotence**; is a ***persistent*** (at least 6 months) **sexual dysfunction** *characterized by* the ***inability*** to **develop** or **maintain** an **erection** of the **penis** *during* **sexual activity**.
- **Prevalence:-**
  - The ***incidence*** is **low** in **men** *younger than* **40 years** of **age**.
  - **Erectile dysfunction** (ED) ***affects*** **50%** of **men** ***older than*** 40 **years**.
- **Physiology:-**
  - **Normal Penile Erection**;
    - ***Requirements***;
      - **Physiological**; **vascular**, **nervous** and **hormonal**.
      - **Psychological**; **sexual stimuli**.
    - ***Mechanism***;
      - **Reflex erection**; *achieved by* ***directly*** **touching** the **penile shaft**.
      - **Psychogenic erection**; *achieved by* **erotic** or **emotional stimuli**.
    - ***Anatomy***;
      - ***Two* corpora cavernosa** on the ***dorsal side*** → ***fill*** with **blood** → **erection**.
      - ***One* corpus spongiosum** on the ***ventral side***.
    - ***Erection Induction***;
      - Sexual stimuli → release of nitric oxide (NO) → activate guanylate cyclase (GC) → ↑ cyclic guanosine monophosphate (cGMP) → ↓ Ca^{2+} influx → relaxation of vascular smooth muscle → vasodilatation → blood filling of the corpora ☞ **Erection**.
    - ***Erection Maintenance***;
      - Maintenance of erection during sexual activity by; ↓ venous outflow from the corpora, which is caused by compression of subtunical venules against the tunica albuginea by the swollen corpora.


Flaccid: Lateral view
Flaccid: Transverse view
Penile venules (uncompressed)
Deep dorsal vein
Corpora cavernosa
Cavernosal arteries
Spongy urethra
Prepuce
Corpus spongiosum
Erect: Lateral view
① Cavernosal arteries dilate, engorging corporal tissue with blood
② Engorging causes corporal tissue to swell, erecting the penis
Erect: Transverse view
③ Engorged corporal tissue compresses penile veins and venules, maintaining erection

➢ DSM-5 Diagnostic Criteria:-

- At ***minimum* 1 of the following** for ***at least* 6 months**;
  1) ***Marked difficulty*** in **obtaining** an **erection *during*** **sexual activity**.
  2) ***Marked difficulty*** in **maintaining** an **erection *until*** the **completion** of **sexual activity**.
  3) ***Marked decrease*** in **erectile rigidity**.

➢ Causes:-

Vascular	Atherosclerosis Peripheral vascular disease Myocardial infarction Arterial hypertension Vascular injury from radiation therapy Vascular injury from prostate cancer treatment Blood vessel and nerve trauma Medications for treatment of vascular disease
Neurologic	Epilepsy Stroke Multiple sclerosis Guillain-Barré syndrome Alzheimer disease Trauma
Penile	Peyronie disease Epispadias Priapism
Nutritional	Malnutrition Zinc deficiency
Surgical	Brain and spinal cord procedures Retroperitoneal or pelvic lymph node dissection Aortoiliac or aortofemoral bypass Abdominal perineal resection Proctocolectomy Transurethral resection of the prostate Radical prostatectomy Cryosurgery of the prostate Cystectomy
Systemic	Scleroderma Renal failure Liver cirrhosis Idiopathic hemochromatosis Cancer and cancer treatment Dyslipidemia Hypertension Chronic obstructive pulmonary disease Sleep apnea Sickle cell anemia
Endocrine	Hypogonadism Diabetes mellitus Hyperthyroidism Hypothyroidism
Psychiatric	Depression Widower syndrome Performance anxiety Posttraumatic stress disorder
Medications	Antihypertensives (β-Blockers, Thiazide, Spironolactone and Clonidine) Antidepressants (SSRIs and TCAs). Antipsychotics (*especially* Atypical). Cimetidine 5-Alpha reductase inhibitors (Finasteride and Dutasteride) Cholesterol-lowering agents

➢ Treatments:-

- Lifestyle modifications;
  - **Stop smoking.**
  - **Control diabetes mellitus.**
  - **Control hyperlipidemia.**
  - **Control hypertension.**
  - ***Decrease* alcohol intake.**
  - ***Discontinue* illicit drugs.**
  - **Exercise** and ***Lose* weight.**
  - ***Review* current medications.**
  - **Cardiovascular disease** *must be* **stabilized** and **assessed** *before* **treatment.**

- **Pharmacotherapy**;

Hormone Replacement Therapy

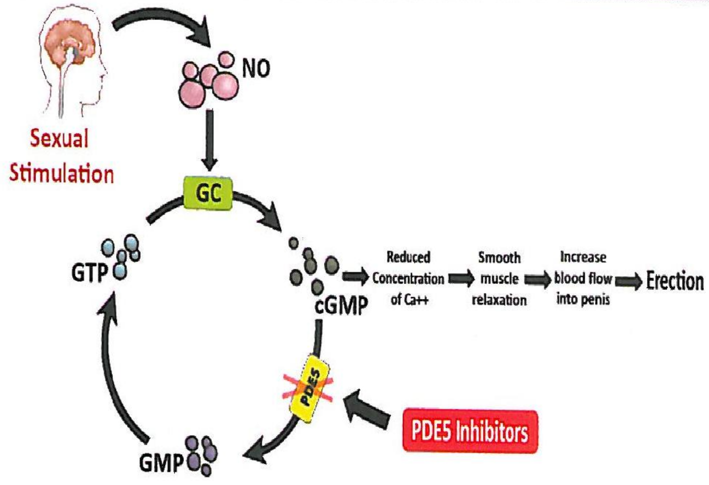
Testosterone

- **Testosterone** *replacement* if **Testosterone** *levels* are *found to be* **low**.
- *Dose and administration*;
    - **Oral Testosterone** ***should not*** be **used** *because* of ***potential*** **liver toxicity**.
    - *Depot* **IM injection** of **Testosterone Enanthate** 200 mg or **Cypionate** 300 mg every 2–3 weeks.
    - **Transdermal patches** (Androderm®) ***placed*** **daily** and **Testosterone 1% gel** (AndroGel®) *applied* **every morning**; ***apply to*** **shoulders**, ***upper*** **arms** ***only*** (*should not be applied to genitals, chest or back*).
    - **Topical solution** (Axiron®): ***apply to*** **underarms** ***once daily***.
    - **Pellet implanted** (Testopel®); ***provides*** **hormone** for **3–4 months**.
    - **Buccal system** (Striant®); *Placed on* **gum tissue** ***twice*** **daily**.
- *Side effects*; ***increase*** **blood pressure**, **acne**, ***enlarged*** **prostate**, **liver** ***toxicity***, **cholesterol** ***changes***, **edema** and **polycythemia**.
- *Contraindication*; **prostate cancer**.
- *Monitoring*; *monitor* **serum Testosterone** *within* 1–3 months and at 6-12 month intervals.
- *If* ***no improvement*** *after* **3 months**, may ***discontinue*** **treatment**.

Phosphodiesterase Type-5 (PDE5) Inhibitors

Sildenafil (Viagra®)

- ***Phosphodiesterase type-5*** (***PDE5***) ***Inhibitor*** are ***first-line*** **drug therapy**.
- **Sildenafil** [sil-DEN-a-fil] is a ***phosphodiesterase type-5*** (***PDE5***) ***Inhibitor***.
- **Early 1990s**; **Pfizer** completes *several early* trials of **Sildenafil** citrate for its use as a **heart disease** ***treatment***, but **volunteers** in the clinical trials are *reporting* ***increased*** **erections** several days after taking a dose of the **Sildenafil**.
- **In 1998** the **FDA approved** Viagra® (**Blue pill**) to *treat* **Erectile Dysfunction (ED)** and **Pulmonary Arterial Hypertension (PAH)**.



Mechanism OF Action

- ***During*** **sexual stimulation** ⇨ ***Stimulate*** release of **nitric oxide** (**NO**) in the **corpus cavernosum** in the **penis**.
- **NO** ***release*** ⇨ ***activate*** **guanylate cyclase** (**GC**) ⇨ ↑ **cyclic guanosine monophosphate** (**cGMP**) ⇨ ↓ Ca^{2+} ***influx*** ⇨ ***relaxation*** of **blood vessels smooth muscle** ⇨ **vasodilatation** ☞ **Erection**.
- **Phosphodiesterase type-5** ***responsible for*** **degradation** of **cGMP** into **GMP**.
- **Sildenafil** is a ***selective*** ***phosphodiesterase type-5*** (***PDE5***) ***Inhibitor*** ⇨ ***accumulation*** of **cGMP** ☞ **Erection**.
- **Sildenafil** has ***no effect*** in **absence** of **sexual stimulation**.

Phosphodiesterase Enzymes

- ***PDE enzyme types***: PDE-1, 2, 3, 4, 5, 6, 7, 8, 9, 10 & 11.

Type	Main function and location
PDE-3	- Control cardiac contractility.
PDE-5	- Control contractility of pulmonary vascular smooth muscle and the corpus cavernosum.
PDE-6	- Control photo-transduction pathway of the retina.

- **Sildenafil** effect is more potent on PDE-5 than other phosphodiesterases.
  - The approximately 4,000 fold selectivity for PDE-5 versus PDE-3.
  - The approximately 10 fold selectivity for PDE-5 versus PDE-6.

Pharmaco Kinetics

- ***Pharmacokinetics***;
  - ***Absorption***; ***rapidly*** **absorbed** (*orally*).
  - ***Maximum*** **plasma concentrations** *within* **30-120 minutes**.
  - ***Metabolism***; ***predominantly*** by **CYP3A4**.
  - ***Excretion***; feces (80%) and urine (13%).

Therapeutic Uses

- *Uses*; - **Erectile Dysfunction (ED)**.
  - **Pulmonary Arterial Hypertension (PAH)**; It relaxes the arterial wall, leading to decreased pulmonary arterial resistance and pressure.
  - **Sildenafil 20 mg** can ***improve*** **fetoplacental perfusion** in **pregnancies**.

Dose

- **Usual Adult Dose for Pulmonary Hypertension**:
  - 20 mg orally three times a day.
- **Usual Adult Dose for Erectile Dysfunction:**
  - 50 mg - 100 mg orally once a day, as needed, 1 hour prior to sexual activity.
- ***Dose Adjustments*** **(erectile dysfunction)**:
  - **Geriatric**: 25 mg 1 hour prior to sexual activity.
  - ***Mild to moderate*** **renal dysfunction**: No adjustment recommended.
  - ***Severe*** **renal dysfunction** (CrCl less than 30 mL/min): 25 mg.
  - **Hepatic impairment** (any degree): 25 mg.
  - With **alpha blockers** or with **CYP450 3A4 inhibitors** (**Ketoconazole** or **Erythromycin**): 25 mg.

Side Effects

- ***Most common adverse effects***:
  - **Headache, flushing, dyspepsia, abnormal vision, nasal congestion, back pain, myalgia, nausea, dizziness** and **rash**.
  - **Abnormal vision**: ***due to*** **inhibition** of **PDE-6**.

**** In Details ****

- **Common**: (10% or more):
  - Headache (28%) dyspepsia (17%), abnormal vision (11%) {green vision/blue vision}
  - Diarrhea (10%), myalgia/back pain (10%), flushing (10%), nasal congestion (10%) and rash (10%).
- **Uncommon** (0.1% to 1%):
  - Tachycardia and hypotension ⇨ transient decreases in supine blood pressure in healthy volunteers (maximum decrease of 8.4/5.5 mmHg).

Contra indication

- In **patients** ***who taking*** **Nitrates**.
- ***Severe*** **hepatic impairment** or ***severe*** **renal impairment**.
- **Hypotension**, ***recent*** **stroke** or **heart attack**.
- **Retinal disorders** (genetic disorders of retinal phosphodiesterases).

FDA Warning

- **Patients** ***should stop*** **Sildenafil** if a **sudden loss of vision** occurs in ***one*** or ***both*** **eyes**, *which could be a sign of* **Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION)**.
- **Patients** ***should stop*** **Sildenafil** in the ***event*** of **sudden** ***decrease*** or ***loss*** of **hearing**.

Vardenafil (Levitra®) | **Tadalafil** (Cialis®)

- **Vardenafil** [var-DEN-a-fil] and **Tadalafil** [ta-DAL-a-fil] are ***selective* PDE-5 inhibitors** *used for* **Erectile Dysfunction**.
- ***Structurally*** **Vardenafil** is ***similar to* Sildenafil**, while **Tadalafil** is ***very different***.
- **Vardenafil** is ***may*** be **effective** in the *treatment of* **Premature Ejaculation**!!
- **Tadalafil** ***used for*** in **treatment of Pulmonary Arterial Hypertension** and ***symptoms of*** **Benign Prostatic Hyperplasia (BPH)**.
- **Vardenafil** is ***more selective*** than **Sildenafil** and **Tadalafil** to **PDE-5**.
- ***Brief comparison***:

	Sildenafil	Vardenafil	Tadalafil
FDA approval date	March 27, 1998	August 19, 2003	November 21, 2003
Dosage form	25mg, 50mg, 100mg tablets	2.5mg, 5mg, 10mg, 20mg tablets	5mg, 10mg, 20mg tablets
Efficacy	82-84%	80%	81%
Onset of action	30 minutes (effect delayed by food)	25 minutes (effect delayed by fatty meal)	16-45 minutes (effect NOT delayed by food)
Recommended dose	50 mg, may be adjusted to 100 mg or 25 mg	10 mg, may be adjusted to 20 mg	10 mg, may be adjusted to 20 mg
Duration of action	4 to 5 hours	4 to 5 hours	36 hours
Food Interactions	- Less effective after high-fat meal	- Less effective after high-fat meal - Moderate-fat meal does not reduce its effectiveness	- Works without regard to what eat
Most common side effects	Facial flushing, headache, indigestion	Facial flushing, headache	Headache, indigestion
Less common side effects	Altered vision, dizziness, nasal congestion	Indigestion, nausea, dizziness, nasal congestion	Back pain, muscle aches, nasal congestion, facial flushing, dizziness

Vardenafil is ***also available*** in an **orally disintegrating tablet (ODT)** *formulation*; ***not*** **affected by a high-fat meal.**

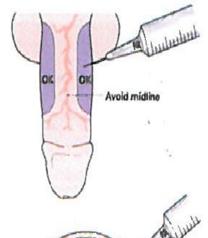
Avanafil (Stendra®)

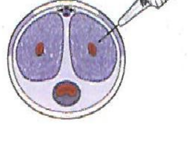
- **Avanafil** [a-VAN-a-fil] is a ***selective*** is a **PDE-5 inhibitor** *approved for* **Erectile Dysfunction** by **FDA** on April 27, 2012.
- ***Onset of action***: **15 minutes** (***Fast onset of action***). - ***Duration of action***: ***up to*** **6 hours**.
- ***Dosage form***: Tablets: 50, 100 and 200 mg. - ***Side effects*** *same as* **Sildenafil**.

Prostaglandin Analogues

Alprostadil (Caverject®)

- **Alprostadil** [al-PROS-ta-dil] is a **prostaglandin** E_1 **(**PGE_1**)** ***analogue*** used in **male erectile dysfunction** (***second-line therapy*** *if* **PDE-5 inhibitors** ***fail***), ***increases*** **cAMP → smooth muscle** ***relaxation***.
- ***Dosage form***: **urethral suppositories** and **injection**.
  - MUSE® **penile suppository**; 125–1000 mcg ***inserted into*** the **urethra**.
  - Caverject®; **2.5-40 mcg injected *directly into* corpus cavernosum**.
- ***Onset of action***: **5-10 minutes**.
- ***Duration of action***: ***Injection*** ⇨ **1-3 hours**, ***supp.***⇨ **30-60 minutes**.
- ***Common side effects***: **penile pain** (*place of injection*) or **urethral pain** (*suppository only*), **priapism** and **hypotension**.





- **Priapism**; **erect penis *does not* return to its flaccid state, *potentially* painful** and is ***considered*** **a medical emergency; Phenylephrine, Pseudoephedrine, Terbutaline** and **Methylene blue can be used.**
- ***Drug interactions***: ***Not used*** *with* **PDE inhibitors**.
- ***Topical* Alprostadil cream** (Vitaros®) has been ***approved in* Canada** as a ***first-line treatment* ED**.

Other (off-label)

Yohimbine (Yohimbex®)

- **Yohimbine** [yoh-HIM-bean] is a ***selective competitive*** **α_2-blocker**.
- It is a ***natural alkaloid*** *derived from* the bark of the ***yohimbe*** **tree** in Central Africa.
- *Uses*: **mydriatic**, **erectile dysfunction** and as **fat burner** (***promoting*** **lipolysis**; Lipo 6®).
- *Dose*; 5.4 mg orally 3 times daily.
- *Mechanism of action*: The **exact mechanism** for its **use** in **impotence** has ***not*** been **fully elucidated**.
  - Yohimbine ***blocks*** **central** ***pre-synaptic*** **α_2-adrenergic receptors** ⇨ ***leads*** to ↑ **release** of **neurotransmitters** in **CNS** and in **corpora cavernosum penis** such as **nitric oxide (NO)**, **noradrenaline** & **dopamine**.
- *Common side effects*: **Tachycardia**, **hypertension**, ***increased*** **motor activity**, **tremor** and **dizziness**
- In **1983**, **Penile erection** could be *induced by* the ***Intracavernosal injection*** of **vasoactive drugs** such as **Papaverine**, **Phentolamine** and **Phenoxybenzamine**.

Papaverine (Papacon®)

- **Papaverine** [pa-PAV-er-een] is an ***opium alkaloid*** **antispasmodic drug**, ***used*** *primarily* in the ***treatment*** of **visceral spasm**, **vasospasm** and in the ***treatment*** of **erectile dysfunction**.
- *Mechanism* (not clear); **Papaverine** is a ***non-specific*** **phosphodiesterase inhibitor**.
- **Papaverine** ***injection*** (**Intracavernosal**) and **topical gel** is *also* **available**.
- *Dose*; 7.5-60 mg **Intracavernosal injection**.
- *Common side effects*: **Priapism**, **corporal fibrosis**, **hypotension** and **hepatotoxicity**.

Phentolamine (Rogitine®)

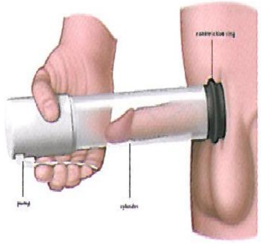
- **Phentolamine** [fen-TOL-a-meen] are **non-selective** ***reversible competitive*** **α-antagonist**.
- *Administration*; **intracavernosal injection**.
- **Phentolamine** ***monotherapy*** is ***avoided*** because **large doses** are ***required*** for an **erection**, and at these **large doses** can cause ***systemic*** **hypotension**.
- *Combination between* **Phentolamine** and **Papaverine** are considered ***safer*** and are *associated with* the **potential** for ***fewer*** **serious side effects** than **high doses** of any **one** of ***these*** agents.
- *Common side effects*: **Priapism**, **corporal fibrosis** and **hypotension**.

Apomorphine (Ixense®) (Uprima®)

- ***Sublingual*** **Apomorphine** has ***demonstrated*** some ***benefit*** in **erectile dysfunction**.

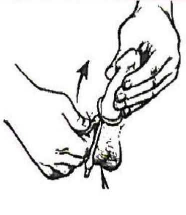
- **Device Therapy**;

Vacuum Erection Devices; VEDs (Penis Pump)



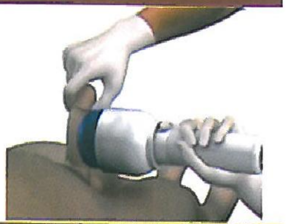
- **Vacuum Erection Devices (VEDs)** *helps* ***draw*** **blood** *into the* **penis** by ***applying*** **negative pressure** and ***used*** *before* **sexual intercourse**.
- *Several types* of **FDA approved vacuum therapy devices** are *available*.
- **VEDs** may be used as ***second-line therapy*** in **patients** who ***not*** **respond** to ***oral*** and ***injectable*** drug *treatments for* **erectile dysfunction**.
- **Vacuum pump devices** ***used*** when **pharmacological methods** are ***fails***.
- *Side effects*; **pain**, **bruising** and ***excessive*** **vacuum** *cause* **vascular damage**.

Venous Constriction Rings



- ACTIS® ***device*** is *designed to* ***enhance*** **erections** by ***slowing*** the **flow** of **blood** ***away from*** the **penis**, which **aids** the ***normal*** **erection process**.
- *Contraindications*; **sickle cell anemia**, **leukemia** or **conditions** that either ***increase*** or ***decrease*** **blood clotting**.

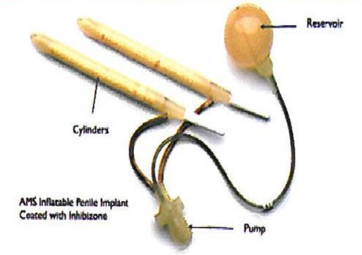
Shockwave Therapy

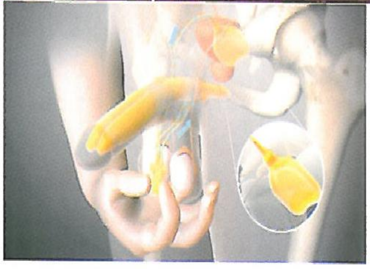


- **Low-intensity extracorporeal shock wave therapy** (**LI-ESWT**) is a ***novel device*** that has ***recently*** been ***developed for*** treating **erectile dysfunction**.
- **LI-ESWT** ***uses*** **energy** to *trigger* a process called ***neovascularization*** (new blood vessel formation in abnormal tissue) that it ***aims*** to ***restore*** the ***normal*** **erectile mechanism**.

Penile Implant (Penile Prosthesis)

- **Device** is ***surgically*** **implanted** ***within*** the **corpora cavernosa** of the penis to ***allow manually*** **erection**.





4) Female Orgasm Disorder (FOD)

Overview:-

- **Woman's orgasm** may *last* ***slightly*** **longer** or ***much*** **longer** *than* a **man's**.
- **Women's orgasms** have been *estimated to* **last**, on average, *approximately* **20 seconds** and to ***consist of*** a **series** of **muscular contractions** in the **pelvic area** (vagina uterus and anus).
- **Female Orgasmic Disorder** (**FOD**); *involves* **difficulty** in ***achieving*** **orgasm**, ***substantially decreased*** **intensity** of **orgasm** or **both**.
- **Anorgasmia** is a *type* of **sexual dysfunction** in which a person **cannot** **achieve orgasm** *despite* **adequate stimulation**.
- **Anorgasmia in males** or **Male Orgasmic Disorder** (**MOD**), it is ***most closely*** *associated with* **delayed ejaculation** (*see next*).

Prevalence:-

- *Reported* **prevalence rates** for **female orgasmic problems** in ***women*** *vary widely, from* 10% to 42% (DSM-5).

DSM-5 Diagnostic Criteria:-

- *Presence* of **1** **of the following** for ***at least*** **6 months**;
  1) ***Marked*** **delay** in, ***marked*** **infrequency** of, or **absence** of **orgasm**.
  2) ***Markedly*** **reduced intensity** of **orgasmic sensations**.

Treatments:-

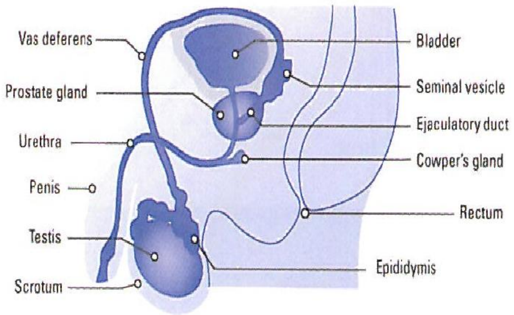
- **Goal**; ***enable*** the **patient** to *reach* **orgasm** as **desired** *under* ***any*** **circumstance** or by **psychotherapy** and/**pharmacotherapy**.
- ***No*** **medication** has been ***specifically*** *approved by* the **US FDA** for the ***treatment*** of **FOD**.
- **FOD** *may be* **treated** with;
  - **Hormonal** to ***correct*** **hormonal imbalances** (*postmenopausal*)
  - **Clitoral Vacuum Pump Devices** (EROS-CTD®) and **Medication** (**Bupropion**, ***topical*** **PDE-5 inhibitors**, ***topical*** **Alprostadil** and ***sublingual*** **Apomorphine**) to ***improve*** **blood flow**, **sexual sensation** and **arousal**.
- **Hitachi Magic Wand device** may use as a **clitoral** ***vibrator*** and is *able to* ***bring*** **women** to **orgasm**.
- **Orgasm control**; *can involve* ***either*** **sex partner** being in **control** of the ***other*** **partner's** **orgasm**, or a ***person*** **delaying** their ***own*** **orgasm** *during* **sexual activity** with a **partner** or by **masturbation** (***any*** **method** of **sexual stimulation** ***can be*** **used**).

5) Ejaculation Problems

Premature | **Retarded** | **Retrograde** | **Absent**

➢ **Overview:-**

- **Erectile dysfunction** and **ejaculatory problems** are the ***most common*** **sexual disorders** in **men**.
- **Ejaculation** is the ***release*** of **semen** from the **penis** ***at*** **orgasm**.
- *At* **orgasm**;
    - Waves of **muscle contractions** ***transport*** the **sperm**, with a *small amount* of **fluid**, from the **testes** *through* to the **vas deferens**.
    - The **seminal vesicles** and **prostate** *contribute* **extra fluid** to ***protect*** the **sperm**.
    - This **mixture** of **sperm** and **fluid** (semen) ***travels*** *along* the **urethra** to the **tip** of the **penis** where it is ***ejaculated*** (released).



- **Men** can *experience* ***different*** **kinds** of **ejaculation problems**, *including*:
    - **Premature ejaculation** (*most common*).
    - **Retarded ejaculation**.
    - **Retrograde ejaculation**.
    - **Absent ejaculation** (*rare*).
- **Painful ejaculation**; *Any* **condition** that *causes* **inflammation** or an **infection** of the **organs** *involved* in **ejaculation** or the ***surrounding*** **structures**, such as **prostatitis**, *may cause* **painful ejaculation**.

Premature (Early) Ejaculation (PE)

➢ **Overview:-**

- **Premature** (*early*) **ejaculation** is the ***most common*** **sexual disorder** in **men** ***younger than*** **40 years**, with **30-70%** of **males** in the **US** ***affected to*** *some* **degree** at **one time** or **another**.
- It has ***historically*** been *considered a* **psychological disease** with ***no identified*** **organic cause**.
- **Men's** ***typical*** **ejaculatory** ***latency*** is *approximately* **4-8 minutes**.
- The **causes** of **premature ejaculation** are ***unclear***.
- **Premature ejaculation** *may* be ***caused by*** **prostatitis** or as a **drug** ***side effect***.

➢ **New Definition (DSM-5 & 2014 ISSM):-** International Society for Sexual Medicine

- **Ejaculation** ***occurring*** *within* ***approximately*** **1 minute** of **vaginal** ***penetration***.

➢ **Prevalence (DSM-5):-**

- ***More than*** **20-30%** of **men** ***ages*** **18-70 years** *report* **concern** *about* ***how rapidly*** they **ejaculate**. ***Only*** **1-3%** of **men** *would be* **diagnosed** *with* the **disorder**.

➢ **Classification:-**

- **Lifelong**; the **disturbance** has been ***present*** *since* the **individual** *became* **sexually active**.
- **Acquired**; the **disturbance** began ***after*** a **period** of *relatively* ***normal*** **sexual function**.

➢ **Severity (DSM-5):-**

- **Mild**: **Ejaculation** *occurring* ***within*** *approximately* **30 seconds** to **1 minute** of **vaginal penetration**.
- **Moderate**: **Ejaculation** *occurring* ***within*** *approximately* **15-30 seconds** of **vaginal penetration**.
- **Severe**: **Ejaculation** *occurring* ***prior*** to **sexual activity**, at the ***start*** of **sexual activity**, or ***within*** *approximately* **15 seconds** of **vaginal penetration**.

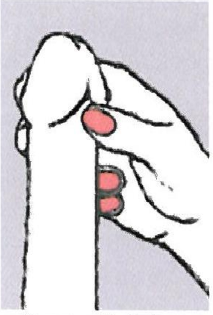
➢ DSM-5 Diagnostic Criteria:-

- For *at least* **6 months**; ***almost all*** or ***all*** (75-100%) **sexual activity**; **ejaculation** *occurring* **during partnered sexual activity** ***within*** **1 minute** ***after*** **vaginal penetration** and ***before*** the **individual** ***wishes it***.

➢ Treatments:-

- **Counseling**;
  - **Focus *their* attention *away* from the sexual stimulation.**
  - **Masturbate** an **hour** or **two** *before* ***having*** **sex**.
  - *Act* **thrusting** ***more*** **slowly**.
  - **Using *more than* one condom** or **use a *thick* condom**.

- **Sex therapy**; *benefits*; **45–65%** of **men**.
  - **Stop-Start Technique**; Masters and Johnson
    1) Stimulate penis until gain an adequate erection.
    2) Engage in sex as normally would.
    3) When feel desire to orgasm, stop!
    4) Take a break from sex while keeping an erection.
    5) Repeat steps 2-4 times.
  - **Squeeze Technique**; Masters and Johnson
    1) Stimulate penis until gain an adequate erection.
    2) Put fingers in the correct position to squeeze penis (see photo).
    3) Applies this squeeze pressure for 10-20 seconds.
    4) Wait for about 30 seconds.
    5) Repeated several times before ejaculation is allowed to occur.



Squeeze Technique

- **Pharmacotherapy**;

Topical Desensitizing

Lidocaine/Prilocaine (EMLA®)

- **Topical desensitizing products** ***applied*** to the **penis** *about* **20–30 minutes** *before* **intercourse**.
- **Condom** *can* **used** *to* ***minimize*** the **effect** of the **cream** on **vaginal** *sensation*.
- ***Side effects***; **Hypoanaesthesia** of the **penile shaft** and **vaginal numbness** (if a condom is not used or not adequately washed off the penis).
- ***Contraindications***; **man** or ***his*** **partner** has an **allergy** to ***any*** **product component**.

Antidepressants

- The ***most effective*** **pharmacologic therapy** for **premature ejaculation** is **selective serotonin reuptake inhibitors (SSRIs)**.
- ***Some*** **tricyclic antidepressants (TCAs)** have the ***same*** **effect** of **SSRIs**, but have ***more*** **side effects**.
- **Ejaculatory** ***delay*** to **6–20 times** ***greater than*** *before* **medication**.

Clomipramine (Anafranil®)

- **Clomipramine** [kloe-MIP-ra-meen] is a ***tricyclic antidepressants***.
- ***Dose***; - **Daily Therapy**; **25-50 mg/day**.
  - **On-demand Therapy**; **25 mg 4-24 hours** *before* **sexual activities**.
- **Clomipramine** is ***more effective*** for **premature ejaculation** *than* ***many*** **SSRIs**.
- **Clomipramine** now, it *has* ***largely*** been ***replaced by*** **SSRIs** *because* it is ***side effects***; **hypotension, fatigue, dizziness, dry mouth** and **QT prolongation**.

Paroxetine (Seroxat®)	**Sertraline** (Lustral®)
Fluoxetine (Prozac®)	**Escitalopram** (Cipralex®)

- The **SSRIs** may be **used** to ***treat*** **premature ejaculation, patients** *may* **report symptom *improvement*** *within* a **few days** of ***starting*** **therapy**, with ***best*** **effects** noted ***after*** about **4 weeks** of **treatment**.
- ***Mechanism*** (unclear); ***probably*** **revolves** *around* ***activation*** of the **5-HT2C receptor**.

- **Dose**; - **Paroxetine**; *Daily*; **10-40 mg/day**. *On-demand*; **20 mg 3-4 hours** *before* **sexual activities**.
  - **Sertraline**; *Daily*; **25-200mg/day**. *On-demand*; **50mg 4-8 hours** *before* **sexual activities**.
  - **Fluoxetine**; *Daily*; **5-20 mg/day**. - **Escitalopram**; *Daily*; **20-40 mg/day**.
- ***Side effects***; **GI side effects, headache, anxiety, fatigue, and sleep disturbances**.
- ***Mild* erectile dysfunction**, ***reduced* libido** and ***increased* suicide risks** may occur with ***high* doses** and ***long-term* use of SSRIs**.

Dapoxetine (Priligy®) (Joybox®)

- **Dapoxetine** is a ***short-acting* SSRI** and it was the ***first* drug *developed* specially** for the ***treatment* of premature ejaculation** as an **on-demand therapy**.
- **Dapoxetine** is the ***only* approved drug** in the **treatment** of **premature ejaculation**, in ***many* countries** (*not approved in US*).
- **Dapoxetine** is the ***ideal compound*** for the ***treatment of* premature ejaculation**, ***because*** it has a **unique pharmacokinetic profile**; ***rapid* absorption**, ***adequate* availability** at the **target site**, and ***rapid* elimination** and ***minimize*** the *incidence* of **side-effects**.
- ***Dose***; **30-60 mg 1-3 hours** *before* **sexual activities** (**on-demand** ***only***).

Some studies have demonstrated that ***combining* PDE-5 inhibitors *with* SSRIs *provides* better results** in the ***treatment of* premature ejaculation** *than* **using SSRIs alone**

Other Agents

Tramadol (Contramal®)

- **Tramadol** is a **μ receptor *agonist*** and **norepinephrine/serotonin reuptake *inhibitor***.
- **Tramadol** may be ***prescribed*** when **SSRIs *haven't been* effective** in ***treatment of* premature ejaculation**, but ***can't*** be used in ***combination with*** an **SSRI**.
- **Dose**; **50 mg 1-3 hours** *before* **sexual activities** (**on-demand** ***only***).
- **Tramadol** has been ***associated with misuse*** (***delay* ejaculation** and **wakefulness**) and ***abuse***.
- ***Long*-term use** of ***high* doses** of **Tramadol** will ***cause* dependence** and a ***withdrawal syndrome***.

Pindolol (Visken®)

- **Pindolol** is a ***non-selective* β-blockers** used in ***combination*** with **Paroxetine** for **premature ejaculation *refractory to* Paroxetine *alone***.

Retarded (Delayed) Ejaculation (RE)

➤ Overview:-

- **Retarded** (**delayed**) **ejaculation** (**RE**) or **male orgasmic disorder** (**MOD**) is *probably **least*** **common** and ***least* understood**, of ***all*** the **male sexual dysfunctions**.
- In **RE man *does not have* orgasms *at all*** or ***cannot** have* an **orgasm** *until **after*** **prolonged intercourse** which ***might last for*** **30–45 minutes** or **more**.

➤ Definition (DSM-5):-

- ***Persistent*** or ***recurrent*** **delay** in, or **absence** of, **orgasm** ***after*** a *normal* **sexual excitement phase** ***during*** **sexual activity**.

➤ Prevalence (DSM-5):-

- ***Less than*** **1%** of **men** will **complain** of ***problems*** with ***reaching*** **ejaculation** that **last *more than*** **6 months**.

➤ Classification:-

- **Lifelong**; the **disturbance** has been ***present** since* the **individual** *became* **sexually active**.
- **Acquired**; the **disturbance** began ***after*** a **period** of *relatively **normal*** **sexual function**.

➤ DSM-5 Diagnostic Criteria:-

- For ***at least* 6 months**; ***almost all*** or ***all*** (75-100%) **sexual activity**;

  1) Marked *delay* in ejaculation. 2) *Marked infrequency* or *absence* of ejaculation.

➤ Causes:-

- **Physical**; **spinal cord injury, major lymph node surgery, type 1 diabetes, multiple sclerosis** and **bladder** or **prostate surgery**.
- **Medications**; **Antidepressants** (*specifically* **SSRIs**).
- **Known cause**; ***very uncommon***.

➢ **Treatments:-**

- **Sex therapy**; Masters and Johnson
  - *If* **man** can ***reach*** **orgasm** by **self-masturbation**, but ***not through*** **intercourse**;
    - * **First stage**; a man masturbates by self in the presence of his partner.
    - * **Second stage**; after a man learns to ejaculate in the presence of his partner, the man's hand is replaced with the hand of his partner.
    - * **Final stage**; the receptive partner inserts partner's penis into the vagina soon as the ejaculation is felt to be imminent.
- **Pharmacotherapy** (*off-label*); ***No* medication** has been ***specifically*** *approved by* the **US**.

Amantadine (Symmetrel®)

- **Amantadine** is an antiviral agent, was ***by chance*** found to have ***Antiparkinsonism properties***.
- **Amantadine** has ***benefit*** in ***treating*** **delayed ejaculation** by ***potentiate*** **dopaminergic function**.
- *Dose*; - **Daily Therapy**; **100-200 mg** *twice* **daily**.
  - **On-demand Therapy**; **100-400 mg/day** *for* **2 days** *before* **sexual activities**.
- ***Side effects***; **Hypotension, dizziness** and **insomnia**.

Bupropion (Wellbutrin®)

- **Bupropion** is a ***weak*** **norepinephrine-dopamine** ***reuptake*** **inhibitor** (**NDRI**).
- *One* **clinical study** *found* **Bupropion** SR **150 mg** ***once*** **daily** given for **2 months** to **men** with ***lifelong*** **delayed ejaculation** increased ***overall*** **ejaculation** from **"fair to good"** compared with baseline.
- ***Side effects***; ***increased*** **risk of seizures, insomnia, anxiety, headache**, and ***decreased*** **appetite**.

Buspirone (Buspar®)

- **Buspirone** is a ***selective*** **5-HT$_{1A}$ agonist**, which is an **antianxiety agent**.
- **Buspirone** has ***minimal*** **data supporting** ***its*** use for **delayed ejaculation**.

Yohimbine (Yohimbex®)

- **Yohimbine** has been associated with ***improvements*** in **delayed ejaculation**.

Cyproheptadine (Triactin®)

- **Cyproheptadine** also acts as a ***serotonin antagonist*** and ***used*** **off-label** as an **appetite stimulant**.
- **Cyproheptadine** has been associated with ***improvements*** in **delayed ejaculation**.
- ***Dose***; **4-12 mg 3-4 hours** *before* **sexual activities**. ***Side effects***; **drowsiness** and **dizziness**.

Pseudoephedrine

- **Pseudoephedrine** may be ***used for*** **delayed ejaculation** because of its ***agonistic*** **action** on **α receptors** and its *ability to* ***increase*** **norepinephrine**; *easy* **contraction** for **ejaculation**.
- ***Dose***; **60-120 mg 1–2 hours** *before* **sexual activities**.

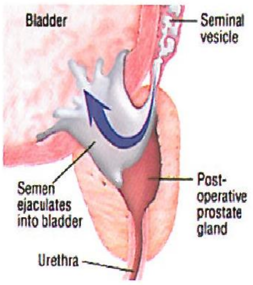
Oxytocin

- **Oxytocin** ***plays*** a **role** in ***regulating*** **orgasms** *through* **several pathways**.
- ***Dose***; **24 international units** of ***intranasal*** **Oxytocin** *just* **minutes** *before* **sexual activities** (quick onset of action) has been suggested for *possible* ***treatment*** of **delayed ejaculation**.

Retrograde Ejaculation

➢ **Overview:-**

- **Retrograde ejaculation** occurs when **semen** is *redirected* to the **urinary bladder**. ***Normally***, the **sphincter** of the **bladder** ***contracts*** *before* **ejaculation**, when the **bladder sphincter** does ***not function*** *properly*, **retrograde ejaculation** ***may occur***.
- **Diagnosis** is ***usually*** by **urinalysis**; the **urine** will contain an ***abnormal*** level of **sperm**.
- **Retrograde ejaculation** is *referred to* as a "**dry orgasm**".
- **Retrograde ejaculation** is *one cause* of **male infertility**.



➢ **Medications:-**

Imipramine	Pseudoephedrine	Chlorpheniramine

- *These* **medications** *can be* **used** in **retrograde ejaculation**, *because* are ***tighten*** the **bladder neck muscles** and ***prevent*** **semen** from **going** *backwards into* the **bladder**.
- ***Usually*** **taken** *at least* **1–2 hours** *before* **sexual activities**.

6) Female Sexual Pain Disorders

- **Female Sexual Pain Disorders** or **Dyspareunia**; is ***painful*** **sexual intercourse**.
- ***Common*** **causes** of **dyspareunia**;
  - **Infections**; **Infections** in the **labia**, **vagina** or ***lower*** **urinary tract**.
    - **Honeymoon cystitis**; Is an infection by *E.coli* can occur when a **woman** has sex for the ***first time***, or when a woman has sex after a long period of time without any sexual activity.
  - **Atrophic vaginitis**; ***thinning***, ***drying*** and ***inflammation*** of the **vaginal walls** due to ***less*** **estrogen** in the **body** in ***postmenopausal*** **women**.
    - **Estrogen therapy**, both ***systemic*** and ***topical***, is the ***most effective*** treatment for **atrophic vaginitis**.
  - **Vestibulodynia** (**Vulvar Vestibulitis Syndrome**); **Pain** which is limited specifically to the **vulvar vestibule**.
  - **Interstitial cystitis** (**painful bladder syndrome**); is a ***chronic*** **disease** characterized by **bladder pain**, **frequency**, **nocturia**, and **urinary urgency**.
  - **Pelvic masses**; **ovarian cysts**, **tumors**, and **uterine fibroids** can cause ***deep*** **pain**.
  - **Endometriosis**; ***most common*** cause of ***chronic*** **pelvic pain** in **women**.

Sexual Transmitted Diseases (STDs)

Genital Herpes (*Herpes Simplex Virus*; HSV Infection)

- ***Herpes simplex virus* 1** and **2** (**HSV-1** and **HSV-2**); are *two* members of the **herpesvirus** ***family***.
- **Symptoms**; **itching**, **genital** ***burning***, **vesicle** ***formation*** and **ulcer** ***formation*** (genital herpes).
- ***About*** 50- 80% of patients have ***recurrent*** **infections** (*generally less severe and of shorter duration*).
- **Treatment**; **2015 STDs Guidelines** *from* **Centers** for **Disease Control** and **Prevention** (**CDC**).
  - **Acyclovir 400 mg** orally 3 times daily for 7–10 days.
  - OR **Acyclovir 200 mg** orally 5 times daily for 7–10 days.
  - OR **Valacyclovir 1 g** orally 2 times daily for 7–10 days.
  - OR **Famciclovir 250 mg** orally 3 times daily for 7–10 days.

Syphilis

- **Syphilis** is a caused by the **bacterium** *Treponema pallidum*.
- **Symptoms** & **Treatments**; **2015 STDs Guidelines** *from* **Centers** for **Disease Control** and **Prevention** (**CDC**).
  1) **Primary syphilis**; *from* **10-90 days** ***after*** **exposure** (*mean* = 21 days); **skin lesion**, called a **chancre**, appears at the **point** of **contact**, **chancre** ***resolves*** *spontaneously* in 2–6 weeks even ***without*** **treatment**.
     - ***Treatments***;
       - **Benzathine Penicillin G** 2.4 million units IM in a single dose (adults).
       - *If penicillin allergy*: **Doxycycline** 100 mg orally twice daily or **Tetracycline** 500 mg 4 times daily for 2 weeks.
  2) **Secondary syphilis**; *from* **4-10 weeks** ***after*** **exposure**; **skin lesions** on the **palms** and **soles**.
     - ***Treatments***; *same as* **Primary syphilis**.
  3) **Latent syphilis**; ***more than*** **1 year** in **duration**.
     - ***Treatments***;
       - **Benzathine Penicillin G** 2.4 million units IM every week for 3 weeks.
       - *If penicillin allergy*: **Doxycycline** 100 mg orally twice daily or **Tetracycline** 500 mg 4 times daily for 4 weeks.
  4) **Tertiary syphilis**; Infectious granulomas and cardiovascular effects.
     - ***Treatments***; *same as* **Latent syphilis**.

Chlamydia Infection

- **Chlamydia infection** is a caused by the **bacterium** *Chlamydia trachomatis.*
- **Chlamydia** is one of the ***most common*** **sexually transmitted infections** worldwide affecting about **4.2%** of **women** and **2.7%** of **men**.
- **Chlamydia infection** Can lead to **pelvic inflammatory disease** (**PID**), **ectopic pregnancy** and **infertility**.
- **Symptoms**;
  - **Women**; ***abnormal*** **vaginal bleeding** or **discharge**, **abdominal pain**, **painful sexual intercourse** (**dyspareunia**), **fever** and **painful urination** (**dysuria**).
  - **Men**; **urethral inflammation** (*painful or burning sensation during urination*; **dysuria**), ***unusual*** **penile discharge** and **testicular pain** or **swelling**.
- **Treatments**; **2015 STDs Guidelines** *from* **Centers** for **Disease Control** and **Prevention** (**CDC**).
  - **Azithromycin 1 g** in a ***single dose*** OR **Doxycycline 100 mg** ***twice*** **daily** for **7 days**.
  - *Alternatives*: **Erythromycin base** 500 mg orally 4 times daily for 7 days OR **Erythromycin ethylsuccinate** 800 mg orally 4 times daily for 7 days OR **Ofloxacin** 300 mg orally twice daily for 7 days OR **Levofloxacin** 500 mg/day orally for 7 days.
  - **Abstain** *from* **sexual intercourse** for *at least* **7 days** and *until* **sexual partners** are ***adequately*** **treated**.

Gonorrhoea (Gonococcal Infection)

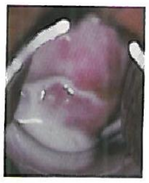
- **Gonococcal infection** is a caused by the **bacterium** *Neisseria gonorrhoeae.*
- **Symptoms**;
  - **Women**; *often* **asymptomatic**, *may include* **vaginal discharge** and **dysuria**.
  - **Men**; **penile discharge** and **dysuria**.
- **Treatments**; **2015 STDs Guidelines** *from* **Centers** for **Disease Control** and **Prevention** (**CDC**).
  - ***Uncomplicated*** **gonococcal infections** of **pharynx**, **cervix**, **urethra** and **rectum**;
    - ***Single doses*** of **Ceftriaxone** 250 mg IM **+ Azithromycin 1 g**.
    - *Alternative*; ***single doses*** of **Cefixime** 400 mg orally **+ Azithromycin 1 g**.
    - ***Allergy*** to **cephalosporins**; ***single doses*** of ***oral*** **Gemifloxacin** 320 mg **+** ***oral*** **Azithromycin 2 g**.
    - **Abstain** *from* **sexual intercourse** for *at least* **7 days** and *until* **sexual partners** are ***adequately*** **treated**.

Pelvic Inflammatory Disease (PID)

- **Pelvic Inflammatory Disease** (**PID**); is an ***infection*** of the **upper part** of the **female** ***reproductive system***.
- ***Untreated*** **PID** can result in ***long term*** **complications** including; **infertility**, **ectopic pregnancy**, **chronic pelvic pain** and **cancer**.
- *Causes*; *Neisseria gonorrhoeae* or/and *Chlamydia trachomatis* are present in 75-90% of cases.
- **Symptoms**; **Fever**, **cervical motion tenderness**, ***lower*** **abdominal pain**, **abnormal discharge**, **painful intercourse** (**dyspareunia**), **uterine tenderness** or **irregular menstruation**.
- ***Elevated*** **erythrocyte sedimentation rate** (**ESR**) and **C-reactive protein**.
- **Treatments**; **2015 STDs Guidelines** *from* **Centers** for **Disease Control** and **Prevention** (**CDC**).
  - **Parenteral Regimens**; discontinued 24 hours after clinical improvement and changed to oral therapy for 14 days.
    - **Cefotetan** 2 g IV every 12 hours **+ Doxycycline** 100 mg orally or IV every 12 hours
    - OR **Cefoxitin** 2 g IV every 6 hours **+ Doxycycline** 100 mg orally or IV every 12 hours
    - OR **Clindamycin** 900 mg IV every 8 hours **+ Gentamicin** loading dose IV or IM (2 mg/kg), followed by a maintenance dose (1.5 mg/kg) every 8 hours.
    - *Alternative*; **Ampicillin/Sulbactam** 3 g IV every 6 hours **+ Doxycycline**100 mg orally or IV every 12 hours.
  - **Intramuscular/Oral Regimens**;
    - **Ceftriaxone** 250 mg IM in a ***single dose*** **+ Doxycycline** 100 mg orally twice a day for 14 days ***WITH*** or ***WITHOUT*** **Metronidazole** 500 mg orally twice a day for 14 days.
    - **Cefoxitin** 2 g IM in a ***single dose*** and **Probenecid**, 1 g orally administered concurrently in a ***single dose*** **+ Doxycycline** 100 mg orally twice a day for 14 days ***WITH*** or ***WITHOUT*** **Metronidazole** 500 mg orally twice a day for 14 days.

Bacterial Vaginosis (BV)

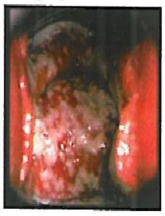
- **Bacterial Vaginosis** (**BV**); is a **disease** of the **vagina** *caused by* ***disequilibrium*** in the ***normal*** **vaginal bacteria**
- ***Causes***; ***reduction*** in *Lactobacilli* and ***overgrowth*** of other organisms usually *Gardnerella vaginalis, Mobiluncus, Bacteroides* and *Mycoplasma.*
- **Symptoms**;
    - ***More than*** **50%** with **bacterial vaginosis** ***asymptomatic*** and usually *without* ***significant*** **irritation** or **erythema.**
    - ***Abnormal*** **vaginal discharge**;
        - **Off-white** ***discharge.***
        - **Thin** and **homogenous.**
        - **Foul-smelling "*fishy*" vaginal odour.**



- **Diagnosis**; **Whiff amine test** (Vaginal discharge + 10% KOH) → Fishy odor (+ve)
- **Treatments**; **2015 STDs Guidelines** *from* **Centers** for **Disease Control** and **Prevention** (**CDC**).
    - ***Non-pregnant women***;
        - **Metronidazole** 500 mg orally twice daily for 7 days.
        - OR **Clindamycin** 2% cream, 1 full applicator intravaginally at bedtime for 7 days.
        - OR **Metronidazole** 0.75% gel one full applicator intravaginally once daily for 5 days.
        - ***Alternatives***:
            - **Clindamycin** ovules 100 mg intravaginally at bedtime for 3 days.
            - OR **Clindamycin** 300 mg orally twice daily for 7 days.
            - OR **Tinidazole** 2 g orally once daily for 2 days.
            - OR **Tinidazole** 1 g orally once daily for 5 days.
    - ***Pregnant women***;
        - **Metronidazole** 500 mg orally twice daily for 7 days.
        - OR **Metronidazole** 250 mg orally three times daily for 7 days.
        - OR **Clindamycin** 300 mg orally twice daily for 7 days.
- ***Do not*** **use Clindamycin** *cream* ***during*** **pregnancy** because of the ***increased*** **risk** of **preterm deliveries.**
- **Treatment** of **sexual partners** is ***not*** **necessary.**

Vulvovaginal Candidiasis (Vaginal Thrush)

- **Vulvovaginal Candidiasis**; is ***excessive*** **growth** of **yeast** (**fungal organisms** usually *Candida albicans*) in the **vagina** that results in **irritation.**
- **75%** of **women** have ***at least*** **1 episode** (**40-45%** will have ***many*** **episodes**).
- **Symptoms**; **Itching**, **irritation**, **redness**, **swelling**, **vaginal pain** and **soreness**, **dysuria** and **dyspareunia.**
    - ***Abnormal*** **vaginal discharge**;
        - **Little** or ***no*** **discharge.**
        - ***If present***;
            - **White** and **clumpy.**
            - **Thick.**
            - **Cottage cheese appearance.**



- **Treatments**; **2015 STDs Guidelines** *from* **Centers** for **Disease Control** and **Prevention** (**CDC**).
    - ***Therapeutic Regimens***;

Drug	Dose	Length of Therapy
Butoconazole	2% cream: 5 g intravaginally	1 dose
Clotrimazole	1% cream: 5 g intravaginally at bedtime	7–14 days
	2% cream: 5 g intravaginally at bedtime	3 days
Miconazole	2% cream: 5 g intravaginally at bedtime	7 days
	4% cream: 5 g intravaginally at bedtime	3 days
	100-mg vaginal suppository at bedtime	7 days
	200-mg vaginal suppository at bedtime	3 days
	1200-mg vaginal suppository	1 dose
Nystatin	100,000-unit vaginal tablet at bedtime	14 days

Terconazole	0.4% cream: 5 g intravaginally at bedtime	7 days
	0.8% cream: 5 g intravaginally at bedtime	3 days
	80-mg vaginal suppository at bedtime	3 days
Tioconazole	6.5% ointment: 5 g intravaginally	1 dose
Fluconazole	150-mg oral tablet	1 dose

- ***Recurrent* vulvovaginal candidiasis** (**four** or ***more* episodes** a **year**);
    - ***Longer* duration** of **initial therapy**;
        - **7–14 days** of **topical therapy**.
        - 100 150 or 200-mg oral dose of **Fluconazole *every* third day** for a total of **3 doses**.
    - ***Maintenance regimen***; Oral **Fluconazole** 100, 150, or 200 mg/week for 6 months.
- ***Pregnant women***; ***Drugs of choice*** is **topical azole**, *applied for* **7 days**.

Trichomoniasis

- **Trichomoniasis** is an ***infectious disease*** *caused by* the ***parasite*** *Trichomonas vaginalis* (anaerobic, flagellated protozoa).
- *About* **70%** of **women** and **men *do not*** have **symptoms** when **infected**, **symptoms** *occur **typically*** with **5** to **28 days *after* exposure**.
- **Symptoms**;
    - **Women**; **malodorous**, **yellow-green vaginal discharge**, **vaginal irritation** and **strawberry cervix** or **vagina** (20% of cases).
    - **Men**; **often** have ***no* symptoms**.
- **Treatments**; **2015 STDs Guidelines** *from* **Centers** for **Disease Control** and **Prevention** (**CDC**).
    - **Metronidazole** 2 g orally in a ***single dose*** OR **Tinidazole** 2 g orally in a ***single dose***.
    - *Alternative*; **Metronidazole** 500 mg orally twice daily for 7 days.
    - ***All sexual* partners** *should be* **treated**.

Human Papillomavirus (HPV) infection

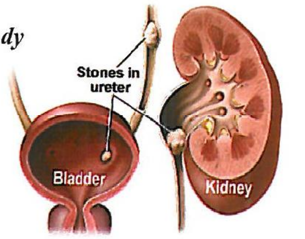
- ***Human papillomavirus* infection** is an ***infection*** by *human papillomavirus* (*HPV*).
- ***Most* HPV infections** cause ***no symptoms*** and ***resolve* spontaneously**.
- **Anogenital warts** or **genital warts**; is a ***types of*** *human papillomavirus* (HPV).
- **HPV *types* 6** and **11** are ***most frequently*** the cause of **genital warts**.
- **Symptoms**; ***usually* asymptomatic**, but ***depending*** on the **size** and **anatomic location**, they can be **painful** or **pruritic**.
- **Treatments**; **2015 STDs Guidelines** *from* **Centers** for **Disease Control** and **Prevention** (**CDC**).
    - ***External Anogenital Warts*** (**penis**, **groin**, **scrotum**, **vulva**, **perineum**, **external anus** and **perianus**);
        - ***Patient-Applied***:
            - **Imiquimod** 3.75% (*every night*) OR 5% (*3 times a week*) **once** at bedtime, *for up to* **16 weeks**
            - OR **Podofilox®** (**Podophyllotoxin**) 0.5% solution or gel; twice a day for 3 days, followed by 4 days of no therapy, this cycle can be repeated, as necessary, for up to four cycles.
            - OR **Sinecatechins** 15% (green-tea extract) ointment; three times daily until complete clearance of warts is achieved (should not be continued for longer than 16 weeks).
        - ***Provider-Administered***:
            - **Cryotherapy** with **liquid nitrogen** or **cryoprobe**.
            - OR **Surgical removal**.
            - OR **Trichloroacetic acid** (**TCA**) or **Bichloroacetic acid** (**BCA**) 80%–90% **solution**.
        - *Alternative*; **Podophyllin resin**, **Interferon**, **photodynamic therapy**, and ***topical* Cidofovir**.
    - **Regimens for Urethral Meatus Warts**; **Cryotherapy** with ***liquid nitrogen*** OR **Surgical removal**.
    - **Recommended Regimens** for **Vaginal**, **Cervical** and **Intra-anal Warts**;
        - **Cryotherapy** with **liquid nitrogen**.
        - OR **Surgical removal**.
        - OR **Trichloroacetic acid** (**TCA**) or **Bichloroacetic acid** (**BCA**) 80%–90% **solution**.
- **Podofilox®** (**Podophyllotoxin**), **Podophyllin**, and **Sinecatechins *should not*** be **used *during* pregnancy**.

HIV/AIDS and **hepatitis** are ***sexually transmitted disease*** and will discussed later (Chemotherapy chapter).

Kidney Stones

➢ Overview:-

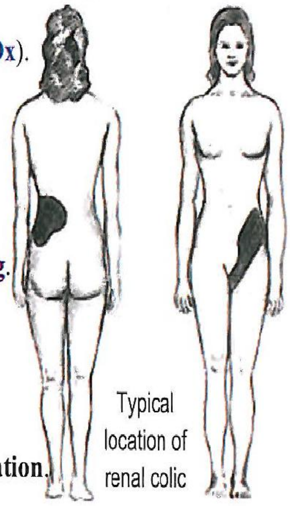
- **Kidney Stones** (**Renal Stones** or **Urolithiasis**); is a **solid** *piece* of **material** (stone or calculi) *occurs in* the **urinary tract**.
- **Kidney stones** *typically* ***form*** in the **kidney** and ***leave the body*** in the **urine stream**.
- A **small stone** *may* ***pass*** **without** *causing* **symptoms**.
- A **large stone** (*more than* **5 millimeters**) can cause ***blockage*** of the **ureter** *resulting in* ***severe lower*** **back pain** or **abdominal pain**.



- **Blood** in the ***urine*** and ***painful*** **urination** are *also* **present**.
- *About* **6%** of **American women** and **12%** of **men** will ***develop*** a **kidney stone** at *some time* in their **life**.
- ***Most*** stones form due to a ***combination of*** **genetics** and **environmental** ***factors***.
- **Stones** are ***typically*** **classified** ***according*** to **location**: **nephrolithiasis** (in the kidney), **ureterolithiasis** (in the ureter), **cystolithiasis** (in the bladder), or ***according*** to **formation** (***such as***; **calcium**, **uric acid**, **struvite**, **cystine**).
- *About* **80%** of **stones** are ***composed of*** **Calcium Oxalate** (**CaOx**).
- *If* stone causes ***no* symptoms** → ***no* treatment** ***is needed***.

➢ Symptoms:- *depend on stone location and size*;

- **Acute renal colic** (one of the strongest pain sensations); ***sudden*** **onset** of ***severe*** **pain** (**colicky**; comes in waves) *originating in* the **flank** and ***radiating*** to the **groin** or to the ***inner*** **thigh**; ***at least*** **50%** of **patients** have **nausea** & **vomiting**.
- **Hematuria**; **pink**, **red** or **brown** ***blood*** in **urine**.
- **Urinary** ***frequency/urgency***, **dysuria**, **stranguria**.
- **Other**; **fever** and **chills**.

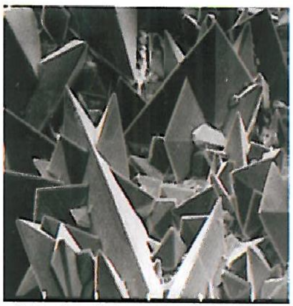

Typical location of renal colic

➢ Risk Factors:-

- **Dehydration** (low fluid intake); is a ***major* factor** in **stone formation**.
- **Dietary**;
  - **Animal Protein**, **Sodium** and **Oxalate**.
  - **Supplemental Calcium** (high intakes of **dietary Calcium** do ***not appear*** to cause **kidney stones** and may actually ***protect*** **against** their **development**).
- **Medical conditions**;
  - **Dent's disease**; is a ***genetic disease*** that ***affects*** the **proximal renal tubules** (It is *one cause* of **Fanconi syndrome**).
  - **Medullary sponge kidney**; is a ***genetic disease*** *characterized by* **cystic dilatation** of the ***collecting*** **tubules** in ***one*** or ***both*** **kidneys**.
  - **Hyperoxaluria**; is an ***excessive*** **urinary excretion** of **Oxalate**.
  - **Hyperparathyroidism**.

➢ Diagnosis:-

- **Laboratory examination**;
  - **Microscopic urinalysis**; *show* **urinary pH level**, **red blood cells**, **bacteria (pus)**, **leukocytes**, **urinary casts** and **crystals** (*help to **know*** a **type** of **kidney stones**).
  - **Urine culture**; *if* **infection** is *present*.
  - **24-Hour urine profile**; ***measure total*** **daily urinary volume**, **magnesium**, **sodium**, **uric acid**, **calcium**, **citrate**, **oxalate** and **phosphate**.
  - **Blood test**; *show* **uric acid** and **calcium level**.
- **Imaging studies**; **Abdominal X-ray**, **ultrasound** and **computed tomography (CT) scans**.


Scanning electron micrograph of the surface of a calcium oxalate kidney stone

- **Classification:-**

Kidney stone type	Prevalence	Circumstances	Crystal shape	Color
Calcium oxalate	80%	Acidic urine	Envelope	Black/dark brown
Calcium phosphate	5-10%	Alkaline urine	Amorphous	Dirty white
Uric acid	5-10%	Acidic urine	Diamond or barrel	Yellow/reddish brown
Struvite (**Magnesium Ammonium Phosphate**)	10-15%	Infections in the kidney (ammonia-producing bacteria)	Coffin-lid	Dirty white
Cystine	1-2%	Cystinosis; genetic disorder (abnormal accumulation of the amino acid cystine).	Hexagon	Pink/yellow

- **Prevention:-** ***depend on stone type***

- **Calcium Oxalate Stones**;
  - *Lifestyle modifications*;
    - *Adequate* **fluid intake** (2.5–3 L of fluids per day).
    - *Moderate dietary* **calcium** *intake.*
    - *Avoid* **oxalate** *containing* **foods**; **spinach, rhubarb, nuts** and **wheat bran.**
    - *Limit* **animal protein**; ***decrease* animal protein *intake*** → 1) ***increase* citrate *excretion*** 2) ***decrease* urate *excretion*** 3) ***decrease* calcium *excretion*.**
    - *Limit* **sodium** intake; ***decrease* sodium *intake* → *decrease* calcium *excretion*.**
      - Check food labels for ingredients and hidden sodium, such as; Monosodium glutamate (MSG), Sodium bicarbonate (baking soda & baking powder), disodium phosphate, sodium alginate and sodium nitrate or nitrite.
  - *Drug therapy*;
    - A) **Thiazide diuretics**; *Reducing* **calciuria** & **stone** *recurrence* (risk for uric acid stones)
    - B) **Alkalinizing agents**; **Citrate Treatment**

Magnesium Citrate (Epimag®)	**Potassium Citrate** (Urocit-K®)
Citric Acid or Citrate	

1) **Citrate salts**; are ***metabolized by*** **liver** and **kidney** and ***produce*** **Bicarbonate** → *raise* **urine pH** → ***inhibits*** **the formation** and ***growth*** of **CaOx crystals.**

2) **Citrate ion** *bind* **with calcium in urine** → **form** *soluble* **citrate complex** → ***inhibits*** **formation** and *growth* of **calcium crystals.**

- **N.B.**; **Citrate treatment *raise* urine pH**, and this ***may* increase** the ***risk*** for **calcium phosphate stones** if ***urine* calcium *remains* high** and **fluid intake** is ***not maintained*.**
- **Citrocid Magnesium Plus®** (**Citric acid** + **Magnesium** + **pyridoxine**); *Adequate* **quantities** of **B-complex vitamins** and **Magnesium** can *prevent* **calcium oxalate stone formation.**

C) **Allopurinol**; *some* **patients** with **calcium oxalate** *stones* **have hyperuricosuria. Uric acid** *facilitates* **the precipitation** of **calcium oxalate** *crystals.*

- **Calcium Phosphate Stones**;
  - The *common cause*; ***high*** **urine pH** (**alkaline urine**) and **hypercalciuria.**
  - *Lifestyle modifications*;
    - *Adequate* **fluid intake** (2.5–3 L of fluids per day).
    - *Moderate dietary* **calcium** *intake.*
    - *Limit* **animal protein** and **sodium intake.**
  - *Drug therapy*;
    - A) **Thiazide diuretics**; *Reducing* **calciuria** and **stone** *recurrence.*
    - B) **Acidifying urine**; by *large dose* of **Vitamin C.**
    - C) **Citrate Therapy**; is ***controversial*** (*not backed by any trials*);
      - **Benefits**; **Citrate** in the **urine** *forms* a *soluble complex* with **Calcium.**
      - **Risk**; **Citrate** *raise* **urine pH** (*increase* **calcium phosphate stone** *formation*).

- **Uric Acid Stones**;
  - *Lifestyle modifications*;
    - ***Adequate*** **fluid intake** (2.5–3 L of fluids per day).
    - ***Limit*** **Purine-Rich Foods**;
      - **Organ meats**; Liver, kidneys, brain and heart.
      - **Game** (hunting) **meats**; rabbit and venison.
      - **Fish**; herring, mackerel, sardines and sprats.
      - **Seafood**; mussels, shellfish and caviar.
      - **Yeast extracts**; beer (not wine).
      - **High-fructose foods.**

  - *Drug therapy*;

A) **Alkalinizing agents**;

Potassium Sodium Hydrogen Citrate (Uralyt-U®)

Sodium Citrate + Citric Acid (Bicitra®)

- **Citrates** are ***metabolized by*** **liver** and **kidney** and ***produce*** **Bicarbonate** → ***raise*** **urine pH** → **dissolve** and ***inhibits*** **the formation** and ***growth*** **of Uric Acids crystals.**

Piperazine Citrate (Urosolvine®)

- Urosolvine® effervescent; introduced in 1949; contains **Piperazine** ***anthelmintic agent***; increase the solubility of urates, **Colchicine**; brings rapid relief in cases of acute gout attacks and **Atropine**; relieves spasms of the urinary tract.

B) **Allopurinol**; ***decrease*** **Uric Acid production** by ***competitively inhibiting*** **xanthine oxidase enzyme** (*due to structure similarity*).

➢ **Managements:-**

Pain Management

NSAIDs

- **Diclofenac** is often the ***first choice*** **NSAID** for **renal colic.**
- **Diclofenac 75 mg** (3 mL) **injection**, **IM**, ***repeated once*** (***may be given*** **30 minutes** later ***if required***, in the ***opposite side***).
- ***May also*** be ***combined with*** **oral Diclofenac** to a ***maximum*** of **150 mg**, daily, for a ***maximum*** of **two days**. **Oral or rectal Diclofenac, 75-150 mg, daily,** ***can be*** **prescribed.**
- **Diclofenac** is ***contraindicated*** in **patients** who have a **cardiovascular risk**. ***Other*** **NSAIDs**, e.g. **Ibuprofen** or **Naproxen**, ***should provide*** **effective pain management** for ***patients*** with **renal colic** in ***these*** **situations.**

Opioids

- **Morphine 5-10 mg, IM** ***every*** **4 hours**; is an ***alternative*** **treatment** to **NSAIDs**
- **Morphine** is ***preferred*** **over NSAIDs** in **pregnant women.**

Others

- **Paracetamol** and a ***weak opioid***, e.g. **Codeine** or **Tramadol**, *can be* ***prescribed if*** **NSAIDs** or **opioids** are ***not appropriate***.
- **IV Lidocaine** ***more effective*** in ***reducing*** **visceral** and **central** *pain compared to* **opioids** and ***used*** if **opioids** is ***not effective*** or **side effects**, **systemic toxicity** of **Lidocaine** ***may occurs*** because it ***blocks*** **sodium channels** in the **heart** and **brain.**

Antiemetic Therapy

- ***Because*** **nausea** and **vomiting** *frequently* ***accompany*** **acute renal colic, antiemetics** often ***play*** a ***role*** **in renal colic therapy.**
- **Metoclopramide** is the ***only*** **antiemetic** that has ***been*** **specifically studied** in the ***treatment*** of **renal colic.** The ***usual dose*** in **adults** is **10 mg IV** or **IM** ***every*** **4-6 hours** as ***needed***.

Antispasmodic Therapy

- **Antispasmodic** are *often used* in the **management** of **renal colic**, *most commonly* in *combination with* **pain management agents**.
- The *role of* **Hyoscine N-butylbromide** in *facilitating* **ureteral stone** *passage* by *acting as* a **muscle relaxant** has been *investigated* and the **results** *do not support* the **theory**.
- **Hyoscine N-butylbromide** *reduces* the **amount of opioid analgesia** *required* in **renal colic**.
- **Drotaverine** is an **antispasmodic** *without* **antimuscarinic** *adverse effects*.
- **Aminophylline** is a *methylxanthine*, it *relaxes* **smooth muscles**.

Medical Expulsive Therapy (MET)

- **Medical Expulsive Therapy** (**MET**) is a *treatment option* in the *management of* **ureteral stones**.
- **MET agents** can *accelerate* the **passage** of **urinary stones** by *relaxing* **smooth muscle** *without preventing* **peristalsis**.
- **MET** is *useful for* **stones diameter** *less than* **10 mm**.
- **MET**; *includes* **α-blockers**, **Calcium Channel Blockers**, **Corticosteroids** and **Phosphodiesterase-5** (**PDE5**) **Inhibitors**.
- **NSAIDs** *have* **ureteral-relaxing effects** and *can be* **considered** a *form of* **MET**.

* **α-blockers**; **Tamsulosin** is a *selective* α_{1A} **receptor** *antagonist making it* the *most commonly prescribed* **α- blocker**, **Silodosin** is *another selective* α_{1A} **receptor** *antagonist* can be used.

* **Calcium Channel Blockers**; **Nifedipine** is the *only* **calcium channel blocker** that has *shown some* **benefit** in **stone expulsion** (**Tamsulosin** *better than* **Nifedipine**).

* **Corticosteroids**; have been *reported to facilitate* **stone expulsion**.

* **Phosphodiesterase-5** (**PDE5**) **Inhibitors**; *Relaxing* **effects** of **ureteral muscle tension** have been observed in patients *receiving* **Vardenafil**, **Sildenafil**, and **Tadalafil**.

Miscellaneous Agents

* **Antibiotics**; can be **used** if *infections* are **present**, *such as*;

- **Ciprofloxacin** (Cipro®) and **Sulfamethoxazole/Trimethoprim** (Septrin®)

* **Urinary Tract Antiseptics**; can be **used** if *infections* are **present**, *such as*;

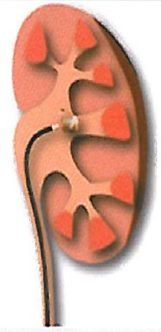
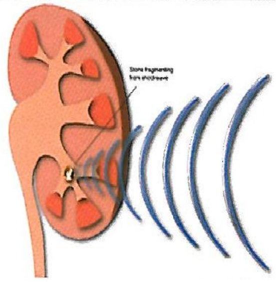
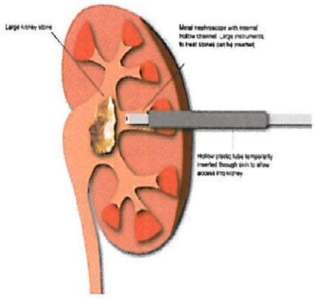
- **Nitrofurantoin** (Uvamin®) *concentrated* in the **urine**, *leading to higher* and *more* **effective levels** in the **urinary tract**, it works by *damaging* **bacterial DNA**.
- **Hexamine** *decomposes* at an **acidic pH** to form **formaldehyde** and **ammonia**, and the **formaldehyde** is *bactericidal*.

* **Other Agents**;

- **Halphabarol** (Proximol®) (*Cymbopogen proximus*) (Halfa bar); is an *antispasmodic* and *used widely* in **management** of **renal colic**.
- **Khellin** (*Ammi Visnaga*); *work by decrease* **calcium oxalate stone** *formation*, **antibacterial** *activity*, *antispasmodic* and *acting as* a **diuretic**.
- Cystone®; *work by decrease* **kidney stone** *formation*, **antibacterial** *activity*, *antispasmodic* and *acting as* a **diuretic**.
- Rowatinex®; *work by* **urinary muscle** *relaxant*, *facilitating* **ureteral stone** *passage* and *decrease* **calcium oxalate stone** *formation*.

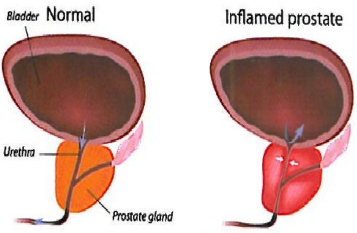
➢ Surgical Therapy:-

- The **2016 American Urological Association** (**AUA**)/**Endourological Society guidelines** ***provide*** ***more specific*** **indications** for **surgical treatment**. The guidelines ***recommend*** surgery in the following scenarios;
  - **Ureteral stones** >10 mm (> 1 cm).
  - ***Uncomplicated*** **distal ureteral stones** ≤10 mm that **have** ***not passed*** *after* **4-6 weeks of observation**, ***with*** or ***without*** MET.
  - **Symptomatic renal stones** in **patients** ***without*** any ***other*** **etiology** for **pain**.
  - **Pediatric patients** with **ureteral stones** that are ***unlikely*** to **pass** or in **whom MET** has *failed*.
  - **Pregnant patients** with **ureteral** or **renal stones** in **whom** ***failed*** **observation** has *failed*.
- **Surgical Options**; **Shockwave lithotripsy** (**SWL**), **Ureteroscopy** and **Percutaneous Nephrolithotomy** (**PCNL**);

	Ureteroscopy	Shockwave lithotripsy (SWL)	Percutaneous Nephrolithotomy (PCNL)
		 Stone fragmenting from shockwave	 Large kidney stone Metal nephroscope with internal hollow channel. Large instruments to treat stones can be inserted Hollow plastic tube temporarily inserted through skin to allow access into kidney
Description	Small flexible camera to enter ureter and kidney. Laser fiber used to fragment stone. Stone fragments are excreted or allowed to pass on their own.	Used focused sound waves from outside the body to fragment a stone. X-ray used to target stone. Patients passes stone fragments.	Small puncture made into kidney directly through skin of back, allows large instruments to be used which can break up and suction out stone fragments.
Best for	- Small to medium stone (1-2 cm). - Multiple stones. - Stones in ureter.	- Stone visible on plan X-ray. - Small to medium stone (1-2 cm).	- Staghorn (Struvite) Stone. - Large stone (> 3 cm). - Some of medium stones.
Benefits	Highest success rate for small to medium stones	Least discomfort	Best option for large stones
Typical operative time	1 hour	½ hour	1-2 hour
Usual Hospital day	Usually none	none	1-2 days
Average day before back to work	9 days	5 days	>1 week
Average day before 100% recovery	16 days	8 days	>2 week

Prostatitis

➢ Overview:-



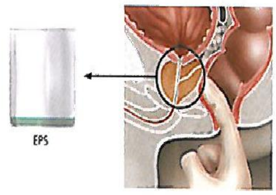
- **Prostatitis**; is an ***inflammation*** of the **prostate gland**.
- **National institutes of health** (NIH) ***classification of*** prostatitis;
  1) ***Acute*** **bacterial prostatitis.**
  2) ***Chronic*** **bacterial prostatitis.**
  3) ***Chronic*** **prostatitis and *chronic* pelvic pain syndrome** (CPPS).
  4) ***Asymptomatic*** **inflammatory prostatitis.**
- ***Acute*** and ***chronic*** **bacterial prostatitis** are ***treated with*** **antibiotic therapy**.
- **CPPS** is *characterized primarily by* **urological pain *without* urinary tract infection**.
- **Asymptomatic inflammatory prostatitis** is *diagnosed during* a ***workup for*** **infertility** or ***elevated*** **prostate-specific antigen** (**PSA**) ***level*** or *after* **WBCs** is ***noted*** in **urine**.
- **Prostatitis** is **one** of the ***most*** **common diseases** seen in **urology practices** in the **United States** (nearly 2 million outpatient visits per year). ***Approximately*** **8.2%** of **men** have **prostatitis** at ***some*** **point** in *their* **lives**.

Category I; Acute Bacterial Prostatitis (ABP)

- **Acute bacterial prostatitis** is a ***serious*** **bacterial infection** of the **prostate gland**.
- ***Symptoms***;
  - **Fever, chills, malaise, arthralgia** and **myalgia**.
  - **Perineal/prostatic pain** (***area between*** the **scrotum** and **rectum**).
  - **Dysuria**.
  - **Obstructive urinary tract *symptoms*** (**frequency, urgency, dysuria, nocturia, hesitancy, weak stream,** and **incomplete voiding**).
  - **Low back pain** and **low abdominal pain**.
- ***Diagnosis***;
  - ** **Midstream** (*middle of bladder*) **urine analysis** and **culture**; ***positive*** **bacteria**.
  - **WBC count** in **urine**; **> 10 HPF**.
  - **Ultrasound** or **computed tomography** (**CT**); in **patients *refractory to*** **initial therapy**.
  - ***Avoid*** **prostatic massage**.
- ***Treatments***; **Therapy duration**: 2–4 weeks.
  - ***Depends on organism***.
  - ***Most frequent regimens***; **Ciprofloxacin** 500 mg twice daily OR **Levofloxacin** 500–750 mg once daily OR **Cotrimoxazole** (**Trimethoprim**160 mg/**Sulfamethoxazole** 800 mg) twice daily.
  - **Hospitalization**; for ***severe*** **cases** of **prostate infection**; **Ampicillin** 2 g IV every 6 hours + **Gentamicin** 5mg/kg every day or 1.5mg/kg every 8 hours.

Category II; Chronic Bacterial Prostatitis (CBP)

- **Chronic bacterial prostatitis** is a ***persistent*** **bacterial infection** of the **prostate gland**.
- *E. coli* is the ***most commonly*** *isolated* **organism**.
- ***Symptoms*** (present for ***at least*** **6 months**);



  - ***No*** **systemic symptoms** (such as; **fever** and **chills**).
  - ***Milder*** **symptoms** *than occur* with **acute prostatitis**.
  - ***Intermittent*** **dysuria**.
  - ***Intermittent*** **obstructive urinary tract *symptoms***.
- ***Diagnosis***;
  - ** **Expressed prostatic secretions** (**EPS**) **analysis**; **EPS sample** is *collected by* **prostatic massage**.
  - **WBC count** in **urine**; **> 10 HPF**.
  - ***No* bacteria** in **urine analysis** and **culture**.

- ***Treatments***; Therapy duration: 4–6 weeks.
  - ***Depends on organism.***
  - ***Most frequent regimens***; *have a good prostate tissue penetration.*
    - ***First-line***; **Ciprofloxacin** 500 mg twice daily OR **Levofloxacin** 500–750 mg once daily (**Fluoroquinolones** *are preferred drugs*) OR **Cotrimoxazole** (**Trimethoprim** 160 mg/**Sulfamethoxazole** 800 mg) twice daily.
    - ***Second-line***; **Doxycycline** 100 mg twice daily OR **Azithromycin** 500 mg thrice-weekly (3-day therapy per week) OR **Clarithromycin** 500 mg twice daily.
- *N.B.*; The ***combination*** of **antimicrobials** and **alpha-blockers** (*such as* **Tamsulosin**) has been suggested to ***reduce*** the ***high*** **recurrence rate.**

Chronic Prostatitis (CP)/Chronic Pelvic Pain Syndrome (CPPS)

- **Chronic prostatitis/chronic pelvic pain syndrome** is ***subdivided into*** **two categories**: **NIH type IIIA** (*inflammatory*) and **IIIB** (*non-inflammatory*).
- ***Differentiation*** *between* **these groups** has been made based on the ***presence*** of **leukocytes (WBCs)** in ***expressed*** and ***post-massage*** **prostatic secretions, urine,** or **semen.**
  - **Inflammatory**; ***Significant*** **WBC count** in the **EPS**, **urine**, or **semen.**
  - **Non-inflammatory**; ***Insignificant*** **WBC count** in the **EPS**, **urine**, or **semen** (**< 10 HPF**).
- The **hallmark symptom** is **pain** attributed to the **prostate** with ***no demonstrable*** **evidence** of **infection.**
- ***Symptoms*** and **Diagnosis**; by
  - **NIH-Chronic Prostatitis Symptom Index (NIH-CPSI)**; This index is calculated using a series of nine questions that contain 21 items used to assess patient history in a standardized and quantifiable format.

* **Pain** or **Discomfort**;

1) In the last week, have you experienced any pain or discomfort in the following areas?

	Yes	No
a) Area between rectum and testicles (perineum)	☐ 1	☐ 0
b) Testicles	☐ 1	☐ 0
c) Tip of the penis (not related to urination)	☐ 1	☐ 0
d) Below your waist, in your pubic or bladder area	☐ 1	☐ 0

2) In the last week, have you experienced;

	Yes	No
a) Pain or burning during urination?	☐ 1	☐ 0
b) Pain or discomfort during or after sexual climax (ejaculation)?	☐ 1	☐ 0

3) How often have you had pain or discomfort in any of these areas over the last week?

☐ 0 Never ☐ 1 Rarely ☐ 2 Sometimes
☐ 3 Often ☐ 4 Usually ☐ 5 Always

4) Which number best describes your AVERAGE pain or discomfort on the days that you had it, over the last week?

0 1 2 3 4 5 6 7 8 9 10
No Pain pain as bad as you can imagine

* **Urination**;

5) How often have you had a sensation of not emptying your bladder completely after you finished urinating, over the last week?

☐ 0 Not at all ☐ 1 Less than 1 time in 5 ☐ 2 Less than half the time
☐ 3 About half the time ☐ 4 More than half the time ☐ 5 Almost always

6) How often have you had to urinate again less than two hours after you finished urinating, over the last week?

☐ 0 Not at all ☐ 1 Less than 1 time in 5 ☐ 2 Less than half the time
☐ 3 About half the time ☐ 4 More than half the time ☐ 5 Almost always

* **Impact of Symptoms**;

7) How much have your symptoms kept you from doing the kinds of things you would usually do, over the last week?

☐ 0 None ☐ 1 Only a little ☐ 2 Some ☐ 3 A lot

8) How much did you think about your symptoms, over the last week?

☐ 0 None ☐ 1 Only a little ☐ 2 Some ☐ 3 A lot

* **Quality of Life**

9) If you were to spend the rest of your life with your symptoms just the way they have been during the last week, how would you feel about that?

☐ 0 Delighted ☐ 1 Pleased ☐ 2 Mostly satisfied
☐ 3 Mixed (about equally satisfied and dissatisfied) ☐ 4 Mostly dissatisfied
☐ 5 Unhappy ☐ 6 Terrible

Scoring the NIH-Chronic Prostatitis Symptom Index Domains

* **Pain**: Total of items 1a, 1b, 1c, 1d, 2a, 2b, 3, and 4 =...........
* **Urinary Symptoms**: Total of items 5 and 6 = ...
* **Quality of Life Impact**: Total of items 7, 8, and 9 =.............

1) Calculate and report 3 separate scores (pain, urinary symptoms, and quality of life)
2) Calculate and report a pain and urinary score (range 0-31);
   Mild =0-9 Moderate =10-18 Severe =19-31
3) Calculate and report total score (range 0-43).

- ***Treatments***; There is ***no preferred* first-line treatment** for patients with **chronic pelvic pain syndrome**.
  - It is ***reasonable*** to try **antimicrobials, alpha blockers,** or **anti-inflammatory *medications***.

A) **Antimicrobials** (*eliminate non-culturable bacteria*); ***First-Line***; **Ciprofloxacin** 500 mg twice daily OR **Levofloxacin** 500–750 mg once OR **Cotrimoxazole** (**Trimethoprim** 160 mg/**Sulfamethoxazole** 800 mg) twice daily; for 4-6 weeks.

B) **α-blockers** (*relief urinary symptoms*); **Tamsulosin** 0.4 mg daily OR **Alfuzosin** 10 mg daily; for 12 weeks.

C) **Anti-inflammatory Agents** (*relief inflammation and pain*); **NSAIDs** & **Corticosteroids** can be used in ***short term***. **Opioids** can be used.

D) **5-α reductase inhibitors** (*promote prostate size reduction*); **Finasteride** 5 mg daily for 6 months.

E) **Phytotherapy**;

Quercetin

- **Quercetin** is a ***polyphenolic bioflavonoid*** commonly ***found in*** **red wine, green tea,** and **onions**. It has ***documented*** **antioxidant** and **anti-inflammatory *properties*** and ***inhibits*** **inflammatory cytokines**.
- ***Dose***; **500 mg *twice* daily *for* 30 days.**
- **DO NOT** ***take*** **Quercetin** for ***more than*** **2 months *without* taking a break.**

Saw Palmetto

- **Saw palmetto** is the ***most commonly*** used **phytochemical** for **lower urinary tract *symptoms*** and **Benign prostatic hyperplasia (BPH)**.
- **Saw palmetto *extract*** is an ***extract*** of the **fruit** of the **saw palmetto** (*Serenoa repens*).

Cernilton

- **Cernilton**, an ***extract*** of **flower pollen**, has been used in **prostatic conditions** for its presumed ***anti-inflammatory*** and ***antiandrogenic effects***.

F) **Pentosan Polysulfate** act by ***replenish*** the **glycosaminoglycan layer** of the **bladder**, ***stabilize*** **prostatic stromal mast cells**. **Dose**; 900 mg daily for 16 weeks.

G) **Muscle relaxants**; **Diazepam** and **Baclofen** are claimed to be ***helpful*** in **sphincter dysfunction** or **pelvic floor/perineal muscle spasm**.

H) **Antineuropathic**; **Pregabalin** OR **Gabapentin** OR **Amitriptyline** OR **Duloxetine** can ***reduce*** **NIH-CPSI total score**.

I) **Botulinum toxin A**; can ***reduce*** **NIH-CPSI total score**.

J) **Physical treatments**; **Electromagnetic therapy, microwave thermotherapy, extracorporeal shock wave therapy, electro-acupuncture** and **myofascial physical therapy**.

K) **Psychological treatment**; such as **cognitive behavior therapy**.

L) **Surgical management**; **transurethral *incision*** of the **bladder neck, radical transurethral resection** of the **prostate** or **prostatectomy**.

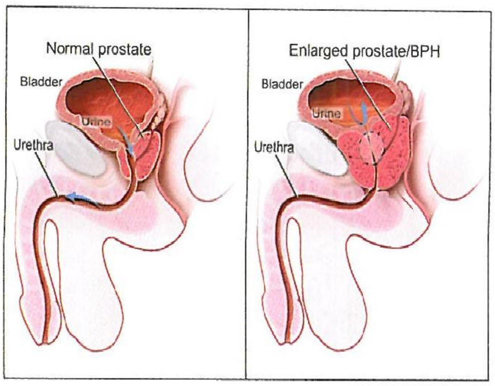
Category IV; Asymptomatic Inflammatory Prostatitis (AIP)

-**Therapy** is ***not indicated***.

Benign Prostatic Hyperplasia (BPH)

➢ Overview:-

- **Benign Prostatic Hyperplasia (BPH)** or **Benign Prostatic Hypertrophy**; is a ***noncancerous*** *increase* in **size** of the **prostate**, is a ***common*** in **older men**.
- **BPH** ***involves*** **hyperplasia** (increase number of cells) ***rather than*** **hypertrophy** (increase size of cells).
- When the **prostate enlarges**, it may ***constrict*** the **flow of urine**.
- *Several* **treatment options** exist to ***treat*** BPH, including **lifestyle changes**, **medications** and **surgery**.


Normal prostate
Bladder
Urine
Urethra
Enlarged prostate/BPH
Bladder
Urine
Urethra

- **BPH** is the ***most common*** cause of **Lower Urinary Tract Symptoms (LUTS)**.

➢ Prevalence:-

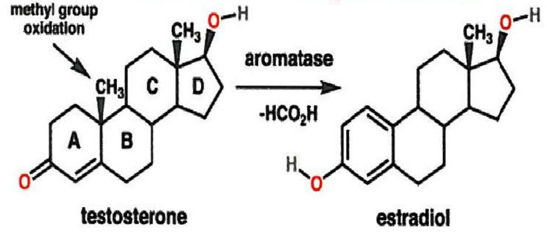
- *About* **one third** of **men** ***older than*** **50 years** have **BPH**.
- *About* **90%** of **men** ***older than*** **85 years** have **BPH**.
- *About* **14 million men** in the **United States** have ***symptoms*** of **BPH**.

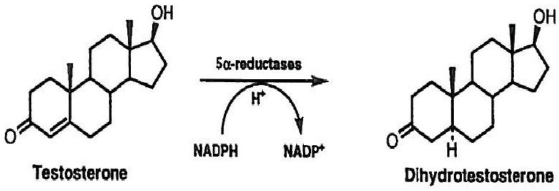
➢ Prostate Function:-

- The ***main function*** of the **prostate gland** is to ***secrete*** an **alkaline fluid** that comprises *approximately* **70%** of the **seminal volume**. The **secretions** *produce* **lubrication** and **nutrition** for the **sperm**.
- The **alkaline fluid** *helps* to **neutralize** the ***acidic*** **vaginal environment**.

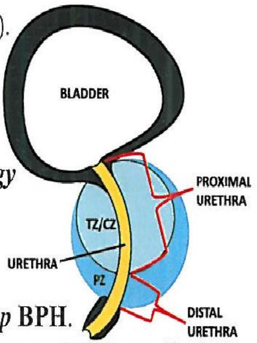
➢ Pathophysiology:-

- *As* **men age**, the *enzymes* **aromatase** and **5-alpha reductase** ***increase*** in **activity**.


methyl group oxidation
CH3
O–H
CH3
A
B
C
D
O
aromatase
-HCO2H
CH3
O–H
H
O
testosterone
estradiol


OH
O
Testosterone
5α-reductases
H+
NADPH
NADP+
OH
O
H
Dihydrotestosterone

- **Aromatase** and **5-alpha reductase** are *responsible for* ***converting*** **androgen hormones** into **Estrogen** & **Dihydrotestosterone (DHT)**.
- **Estrogen** has a key role in the ***growth of cells*** in the **prostate**
- **Dihydrotestosterone (DHT)** is an ***anabolic hormone*** *many times* ***more potent*** *than* **Testosterone**.
- **Estrogen** and **Dihydrotestosterone** when combined, cause a ***synergy*** to *induce* **BPH**.
- **N.B.**; **Men** who are **castrated** *before* **puberty** (castration causes an enlarged prostate to shrink) and **patients** with **type II 5 α -reductase enzyme** (this enzyme found in prostate gland) ***deficiency*** do ***not develop*** **BPH**.
- **Prostatic cancer** *typically* occurs in the **peripheral zone** (PZ). However, **BPH** usually from the **transition zone** (TZ).


BLADDER
PROXIMAL URETHRA
TZ/CZ
URETHRA
PZ
DISTAL URETHRA

➢ Signs and Symptoms:-

- *When the* **prostate *enlarges***, it may act like a **"clamp *on* a hose,"** ***constricting*** the ***flow*** of **urine**. **Nerves** *within the* **prostate** and **bladder** may also ***play*** a **role** in ***causing*** **LUTS**.
  - **Lower Urinary Tract Symptoms (LUTS)**;
    - A) **Storage (Irritative) Symptoms**;
      - **Urinary frequency**; increased frequency of urination.
      - **Urinary urgency**; increased urgency of urination.
      - **Dysuria**; painful urination.
      - **Nocturia**; excessive passage of urine at night.
    - B) **Voiding (Obstructive) Symptoms**;
      - **Poor stream** (unimproved by straining); decreased force.
      - **Hesitancy** (worsened if bladder is very full); a delay between trying to urinate and the flow actually beginning.
      - **Dribbling**; loss of small amounts of urine due to a poor urinary stream.
  - ***N.B.***; **LUTS** as an ***independent*** **risk factor** for **erectile dysfunction** and **ejaculatory dysfunction**.

➢ Diagnosis:-

- **History**; **history of LUTS** and **medications or medical history.**

Medications and medical conditions that may contribute to LUTS in men

Medications

- **α-Adrenergic agonists**; **Decongestants** and **Pseudoephedrine**; increase bladder outlet resistance (increased sphincter tone).
- **Anticholinergics**; **Antispasmodics**, **Antihistamines**, **Tricyclic Antidepressants**, **Phenothiazines**; promoting bladder muscle relaxation.
- **Diuretics**; increase urinary frequency and volume.
- **Testosterone**; stimulate prostate growth.

Medical Conditions

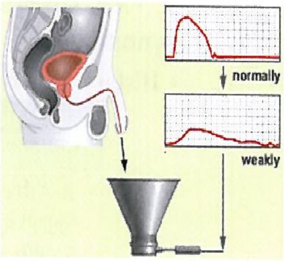
- **Bladder cancer**; mechanical obstruction.
- **Prostate cancer**; mechanical obstruction.
- **Congestive heart failure**; diuresis.
- **Diabetes**; osmotic diuresis and autonomic neuropathy.
- **Parkinson's disease**; autonomic neuropathy.

- **American Urological Association Symptom Index (AUA-SI)**; are ***useful*** **aids** to ***making*** the **diagnosis** of **BPH** and ***quantifying*** the **severity** of **symptoms.**

- A score of 7 or less indicates; **Mild BPH.** - A score of 8 to 19 indicates; **Moderate BPH.** - A score of 20 to 35 indicates; **Severe BPH.**	Not at all	Less than 1 in 5	Less than half the time	About half the time	More than half the time	Almost always
1. Over the past month, how often have you had ma sensation of not emptying your bladder completely after you finished urinating?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
2. Over the past month, how often have you had to urinate again less than two hours after you finished urinating?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
3. Over the past month, how often have you stopped and started again several times when you urinated?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
4. Over the past month, how often have you found it difficult to postpone urination?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
5. Over the past month, how often have you had a weak urinary stream?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
6. Over the past month, how often have you had to push or strain to begin urination?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
	None	1 time	2 times	3 times	4 times	5 times
7. Over the past month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

- ***N.B.***; **American Urological Association Symptom Index (AUA-SI)** has also been ***adopted*** **worldwide** and is ***known as*** the **International Prostate Symptom Score (I-PSS)**.

- **Physical Examination**;
  - **External Genitalia**; should be examined.
  - **Digital** (*finger*) **Rectal Examination (DRE)**; **prostate size** can be ***assessed***, **nodules** can be **evaluated**, and **areas** ***suggestive*** of **malignancy** can be **detected.**
- **Laboratory Studies**;
  - **Urine Analysis**; The **American Urological Association (AUA)** ***recommends*** **urinalysis** for ***all men*** *presenting* with **lower urinary tract symptoms. Urinalysis** *help* ***rule out*** **non-BPH causes** of the **symptoms**, such as **bladder stones** or **urinary tract infection**.
  - **Kidney Function Tests (Blood Urea Nitrogen; BUN, Serum Creatinine)**; ***evaluate for*** **kidney damage** (***not recommended***).
  - **Prostate Specific Antigen (PSA)**; ***marker for*** **an enlarged prostate** ***increasing*** **blood PSA** ***levels*** **in BPH and prostate cancer; 5-α-reductase inhibitors** *reduce* **PSA** in **BPH patients.**
  - **Post-Void Residual (PVR) Urine Test**; *measures* the **amount** of **urine** ***left*** in the **bladder** ***after*** **urination** by *using* **ultrasound** or by **catheterization; > 50 mL, patients** have an ***elevated*** **risk** of **infection.**
- **Imaging Studies** and **Others**;
  - **Transrectal Ultrasonography (TRUS)**; **provides a** ***more accurate*** *assessment* **of prostate volume** than *does* **DRE.**
  - **Uroflowmetry**; is the **electronic** ***recording*** of the **urinary flow** *rate*, an ***abnormally*** **low flow** *rate* may be *caused by* **bladder outlet obstruction (BOO)**
  - **Pressure-Flow Studies** and **Cystometrography**.



Uroflowmetry

➢ Managements:-

1) Watchful Waiting

- **Watchful waiting** is ***recommended*** in **men** who have **mild symptoms** (AUA Symptom Index score of 7 or less).
- The **physician** will ***monitor*** **BPH symptoms** ***periodically*** to **see** *if* they are **stable** or *if* they are **getting worse** (during this time, repeated testing may be performed).
- **Watchful waiting** is often ***recommended*** for *many* **diseases**, because the **majority** of **cases** ***resolve*** **spontaneously**.

2) α_1-Receptor Antagonists

Prazosin (Minipress®)	**Doxazosin** (Cardura®)	**Terazosin** (Hytrin®)
Alfuzosin (Xatral®)	**Tamsulosin** (Flomax®)	**Silodosin** (Rapaflo®)

- **Prazosin** [PRAY-zoe-sin], **Doxazosin** [dox-AY-zoe-sin] and **Terazosin** [ter-AY-zoe-sin] are a ***non-specific selective*** **α_1 blocker**; ***acts on*** **blood vessels** (lower blood pressure) and **prostate** (relax prostate and urethra muscles and relax bladder neck), ***used in*** **symptoms of BPH (LUTS)** and **hypertension**.
- **Alfuzosin** [al-FYOO-zoe-sin] is a ***specific selective*** **α_1 blocker** in the **prostate** and **bladder**, ***approved only*** for **symptoms of BPH (LUTS)**, ***not indicated*** for the **treatment** of **hypertension**.
- **Tamsulosin** [tam-SUE-loh-sin] and **Silodosin** [SIL-oh-DOE-sin] are a ***specific selective*** **α_1 blocker** that has ***preferential selectivity*** for *the* **α_{1A} receptor** in the **prostate** *versus* the **α_{1B} receptor** in the **blood vessels** ***approved only*** for **symptoms of BPH (LUTS)**, ***not indicated*** for the **treatment** of **hypertension**.
- ***All*** **α-blockers** ***relieve*** **symptoms** in **men** ***with*** **moderate** to **severe BPH** (**AUA-SI score ≥ 8**).
- ***All*** **α-blockers** ***lower*** the **AUA-SI** by **4-6 points** in **patients** ***with*** **LUTS** and **BPH**.
- ***Side effects***;
  - ***All*** **α-blockers** can *cause* **orthostatic hypotension** (non-specific >>> specific); Therapy with ***non-specific*** **agents** ***should*** begin at a **low dose** and then be ***titrated*** **upward. Sildenafil** (or ***other*** **PDE-5**) in doses ***greater than*** **25 mg** should not be taken ***within*** **four hours** of **alpha-blocker** use.
  - ***All*** **α-blockers** can *cause* **ejaculation changes, headaches, nasal congestion** and **weakness.**
  - **Patients** *taking* **Tamsulosin** are prone to a ***complication known*** as **floppy iris syndrome** during **cataract surgery**, ***should avoid*** *until* their **cataract surgery** is **completed.**

- Doses;	**Prazosin**	***Start*** at 1 mg twice daily; ***usual*** 2–10 mg in two to three divided doses.
	Doxazosin	***Start*** at 1 mg daily; ***usual*** 1–4 mg daily; ***maximum*** 8 mg.
	Terazosin	***Start*** with 1 mg taken at bedtime; ***usual*** 1–10 mg daily; ***maximum*** 20 mg.
	Alfuzosin	10 mg daily as a single dose.
	Tamsulosin	0.4–0.8 mg daily as a single dose.
	Silodosin	8 mg daily as a single dose - 4 mg daily if CrCl 30–50 mL/minute.

- *Drug interactions*; *All* **α-blockers** are *metabolized through* the **CYP3A4** *pathway* and have **drug** ***interactions*** with ***strong*** **CYP3A4 inhibitors** and **inducers**.

3) 5-a-Reductase Inhibitors

Finasteride (Proscar®)	**Dutasteride** (Avodart®)

- **Finasteride** [fin-AS-ter-ide] and **Dutasteride** [doo-TAS-ter-ide] are a ***5-α-reductase inhibitors***.
- They are inhibits ***5α-reductase enzyme*** which ***convert*** **Testosterone** into the ***more potent androgen*** **Dihydrotestosterone (DHT)** this *lead to* **reduction** in **prostate size** with **improve** in **urinary flow**.
- *Most beneficial*; in **men** *with* **prostates** ***larger than*** **40 g**.
- ***Should not use***; in **men** *with* **LUTS** ***secondary*** to **BPH** ***without*** **prostatic enlargement**.
- *Onset of benefits*; *approximately* **6 months** of **therapy** is *required to* ***achieve*** **clinical benefit**.
- **Finasteride** ***competitively*** **inhibits type II 5-α-reductase**, ***lowers*** **prostatic DHT** by **80%**.
- **Dutasteride** is a ***non-selective inhibitor*** of ***both*** **type I** & **II 5-α-reductase**, ***lowers*** **prostatic DHT** by **94%**; ***No differences*** *between* these **two agents**, ***both reduce*** **prostate size**.
- **PSA** ***concentrations*** are used to ***monitor*** for **prostate cancer**, *because* ***5-α-reductase inhibitors*** ***lower*** **PSA** ***concentrations***.
- *Doses*; **Finasteride**; 5 mg daily. - **Dutasteride**; 0.5 mg daily.
- *Side effects*; ***decreased*** **libido**, **ejaculatory problems** and **erectile dysfunction**.

4) Combination Therapy

Dutasteride + Tamsulosin (CombAT®) (Duodart®) (Jalyn®) (Combodart®)

- *It contains*; **Tamsulosin** 0.4 mg + **Dutasteride** 0.5 mg.
- *Indications*; **severe symptoms** of **BPH** who *also have* an **enlarged prostate** ***larger than*** **40 g**.

5) Phosphodiesterase Type-5 (PDE5) Inhibitors

Tadalafil (Cialis®)

- **Tadalafil** [ta-DAL-a-fil] are ***selective*** **PDE-5 inhibitors** *used for* **Erectile Dysfunction** and it is ***approved for*** use in **BPH** in **2011** or ***both*** **BPH** and **Erectile Dysfunction**.
- *Mechanism* (exact mechanism unknown); is *thought to* be *caused by* ***phosphodiesterase-induced*** **smooth muscle relaxation** in the **bladder**, **urethra** and **prostate**.
- *Doses*; 5 mg once daily. ***Combination of*** **Tadalafil** and **α_1-blockers** is a ***risk of*** **hypotension** ***but*** it can **safe** in **proper instructions**.

6) Antimuscarinics

Oxybutynin (Ditropan®)	**Tolterodine** (Detrusitol®)

- **Oxybutynin** [OX-i-BUE-ti-nin] & **Tolterodine** [tol-TER-oh-deen] ***may use*** to ***improve*** **irritative voiding symptoms** (e.g., **urinary frequency**, **urgency**), which **α_1-blockers** and **5-α-reductase inhibitor** ***does not improve*** **these symptoms**.

7) Phytotherapy or Alternative Therapy

- **Saw Palmetto** (*Serenoa repens*) **extract**; ***most commonly used*** and ***studied***; ***mild*** to ***moderate*** **improvement** in **LUTS**; some of urologists preferred **saw palmetto** over pharmacotherapy.
- **Stinging nettle** (*Urtica dioica*), **South African stargrass** (*Hypoxis rooperi*), **pumpkin seed** (*Cucurbita pepo*), and **African plum** (*Pygeum africanum*); *can be used*, but the **AUA** ***does not*** **recommend** the *use of* **Phytotherapy**.

8) Surgery

- **Surgery** is ***preferred*** in **men** ***with*** **severe symptoms** and in those ***with moderate symptoms*** who have ***not adequately*** **responded** to **medical options**.

Urinary Incontinence (UI)

➢ Overview:-

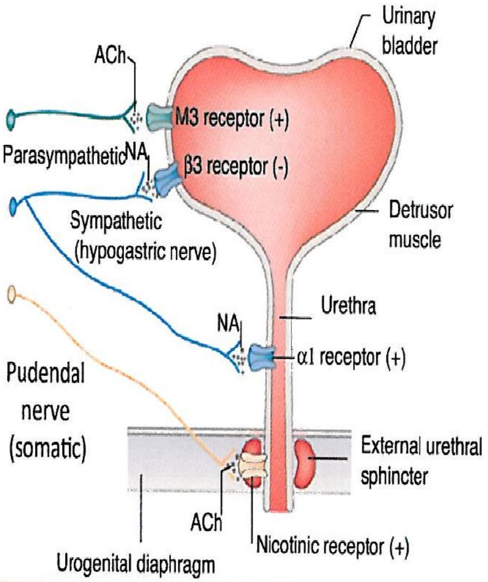
- **Urinary Incontinence** (**UI**), also called **Enuresis**; is an ***involuntary urination*** or *any* ***involuntary leakage*** of **urine** (*loss of bladder control*).
- It is a ***common*** and **distressing problem**, which have a ***large impact*** on **quality** *of* **life**.
- **Urinary incontinence** ***affects*** **millions** of **persons**.
- **Enuresis** is *often* **used** to ***refer to*** **urinary incontinence** *primarily in* **children**, such as **nocturnal enuresis** (bed wetting).
- **Patients** who ***have*** **incontinence** are more likely to have **depression**, ***limited*** **social** and **sexual function** & ***dependence*** on **caregivers**.
- **Transient incontinence** is *spontaneously* ***reverses*** *after* the **underlying cause** is ***resolved***.

➢ Prevalence:-

- *About* **10-13 million people** in the **United States** and **200 million people** ***worldwide***.
- It is ***twice*** as **common** in **women** as in **men** (> 80 years of age, both sexes are affected equally).
- It is affects ***up to*** **7%** of **children** (older than 5 years), **10-35%** of **adults** & **50-84%** of **elderly**.

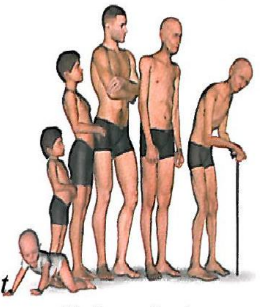
➢ Normal Physiology:-

- **Normal bladder capacity** is **300-500 mL**, and the ***first urge*** to **void** *generally occurs* between bladder volumes of **150** and **300 mL**.
- **Normal bladder emptying**; ***decrease*** **urethral resistance** and ***contraction*** of **detrusor** (**bladder**) **muscles**.
- **Smooth muscles** of the **bladder** and **urethra** are ***innervated by*** **autonomic** and **somatic** ***nerves***;
  - **Sympathetic**;
    - **β₃ receptors** ***stimulation*** → ***relaxes*** **detrusor muscles** → ***increase*** **bladder capacity**.
    - **α₁ receptors** ***stimulation*** → ***increase*** **internal urethral sphincter**.
  - **Parasympathetic**;
    - **M₃ receptors** ***stimulation*** → ***contraction of*** **detrusor muscles** → ***decrease*** **bladder capacity**.
  - **Somatic**;
    - **Nicotinic (N) receptors** (somatic or voluntary) ***stimulation*** → ***increase*** **external urethral sphincter**.


ACh
Urinary bladder
M3 receptor (+)
Parasympathetic
NA
β3 receptor (-)
Sympathetic (hypogastric nerve)
Detrusor muscle
Urethra
NA
α1 receptor (+)
Pudendal nerve (somatic)
External urethral sphincter
ACh
Nicotinic receptor (+)
Urogenital diaphragm

Failures in this control mechanism result in incontinence

➢ Age Effects:-

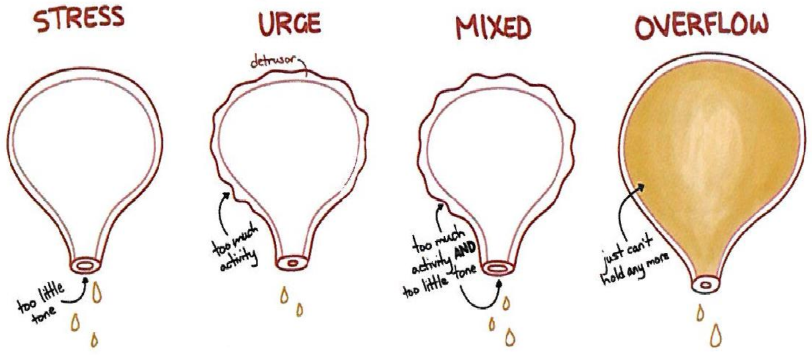


- **Child**; as the **child** ***gets*** **older**, the **nervous system** ***develops***.
- **Elderly**;
  - ***Decreased*** **bladder elasticity** and **capacity**.
  - **Bladder muscles** ***weaken***.
  - ***More frequent*** **voiding**.
  - ***Decrease*** in **flow rate** in **men** with **prostatic** ***enlargement***.
  - ***Decline*** in **bladder outlet** and **urethral resistance** in **women** with ***loss of*** **estrogen**.

➢ Classification:-

- **Transient Urinary Incontinence**; is **urinary leaking** that *spontaneously* ***reverses*** *after* the **underlying cause** is **resolved**.
    - The ***potential*** **causes** of **Transient Incontinence** may be *easily remembered* by the **mnemonic**; **DIAPPERS**;
        - **D**; **Delirium**.
        - **I**; **Infection**.
        - **A**; **Atrophic urethritis** or **vaginitis**.
        - **P**; **Pharmacologic agents**.
        - **P**; **Psychological** and **Prostatitis**.
        - **E**; **Excess urine output** (**Endocrine**).
        - **R**; **Reduced mobility**.
        - **S**; **Stool impaction**.

- **Chronic Urinary Incontinence**; ***does not*** typically ***resolve*** *spontaneously*, and is ***classified into*** five types: **stress**, **urge**, **mixed**, **overflow** or **functional**.



Stress Incontinence

- **Prevalence**; 24-45% in women older than 30 years.
- **Pathophysiology**; **Sphincter *weakness*** (**urethral sphincter** and/or **pelvic floor *weakness***).
- **Symptoms**; ***Loss*** of **small amount** of **urine** *during* **physical activity** or **intra-abdominal pressure** (coughing, sneezing jumping, lifting, exercise); can occur with ***minimal*** **activity**, such as walking or rising from a chair.
- **Causes**; **Childbirth**, **pregnancy**, **obesity** (*in* **women**) and ***after*** **prostatectomy** (*in* **men**).
- **History**; **Patient** *usually* can ***predict*** which **activities** *will cause* **leakage**.

Urge Incontinence – Overactive bladder (OAB)

- **Prevalence**; - **9%** in **women 40** to **44 years** of **age**.
    - **31%** in **women** ***older than*** **75 years**.
    - **42%** in **men** ***older than*** **75 years**.
- **Pathophysiology**; **Detrusor over-*activity*** (***uninhibited*** **bladder contractions**) caused by ***irritation*** *within the* **bladder** or ***loss*** of ***inhibitory*** **neurologic** *control* of **bladder *contractions***.
- **Symptoms**; ***Loss*** of **urine** *preceded by* a ***sudden*** and **severe desire** to **pass urine** (patient typically ***loses*** **urine** ***on the way*** *to* the **toilet**). **Bladder *contractions*** may also be *stimulated by* a ***change in*** **body position** (i.e., from supine to upright) or with **sensory stimulation** (e.g., running water, hand washing, cold weather, arriving at the front door).

- **Causes**;
    - **Bladder irritation (sensory)**; *caused by* **cystitis**, **prostatitis**, **atrophic vaginitis**, **bladder diverticula**, **prior pelvic radiation therapy**.
    - ***Loss of* neurologic control**; *caused by* **stroke**, **dementia**, **spinal cord injury**, **Parkinson disease**.

- **History**;
    - **Volume** of **urine** ***loss*** is **variable**; *ranging from* **minimal** to **flooding**.
    - **Frequency** and **nocturia** ***are common***.
    - **Symptoms** of **urgency** may also occur ***without*** urinary **loss**, which is *known as*; **Overactive Bladder** (**OAB**).

Mixed Incontinence

- **Prevalence**; **20-30%** of **patients** with **chronic incontinence**.
- **Pathophysiology**; ***Combination of*** **stress** and **urge incontinence**.
- **Symptoms**; ***Involuntary*** **leakage** *associated with* **symptoms** of **urgency**; ***loss of*** **urine** *with* **exertion**, **effort**, **sneezing** or **coughing**.
- **Causes**; ***Combination*** of **stress** and **urge incontinence**.
- **History**; **Patient** should **determine** which ***symptom*** is **predominant** and **most bothersome**.

Overflow Incontinence (Urinary Retention)

- **Prevalence**; **5 %** of **patients** with **chronic incontinence**.
- **Pathophysiology**; **Over distention** of the **bladder** caused by ***impaired*** **detrusor contractility** or **bladder outlet *obstruction***; leads to **urine leakage** by ***overflow***.
- **Symptoms**; **Dribbling** of urine, ***inability*** to **empty bladder**, **urinary hesitancy**, **urine loss** ***without*** a **recognizable urge** or **sensation** of **fullness/pressure** in ***lower*** **abdomen**.
- **Causes**; **Anticholinergic medications**, **benign prostatic hyperplasia**, **pelvic organ prolapse**, **diabetes mellitus**, **multiple sclerosis** & **spinal cord injuries**.
- **History**; ***Does not*** *usually* **occur** ***unless*** **bladder emptying** is **poor** (post void residual "PVR" volumes > 200 to 300 mL, indicating incomplete emptying)

Functional Incontinence

- **Prevalence**; Uncertain.
- **Pathophysiology**; ***Variable*** **leakage** of **urine**, usually caused by **environmental** or **physical *barriers*** to **toileting** (Inability to reach the toilet because of mobility constraints).
- **Symptoms**; ***inability to*** **void independently**.
- **Causes**; Caused by **non-genitourinary factors**, such as **cognitive** or **physical impairments**; ***severe*** **dementia**, **physical frailty** or ***inability*** to **ambulate**, **mental health disorder** (e.g., depression).
- **History**; ***Impaired*** **physical function** (**immobility**) and/or ***impaired*** **cognition**.

➢ *Common* Medications Can Cause Urinary Incontinence:-

- **Antihypertensives**;
    - **α-blockers**; decrease sphincter tone → stress incontinence.
    - **ACEIs**; may increase coughing → stress incontinence.
    - **Calcium channel blockers**; relax the bladder and retention → overflow incontinence.
    - **Diuretics**; high urine flow that leads to bladder contractions → urge incontinence.
- **Pain relievers**;
    - **NSAIDs**; increase fluid retention → nocturnal diuresis and functional incontinence.
    - **Opioids**; relax the bladder, fecal impaction, sedation and retention → overflow incontinence.
- **Skeletal muscle relaxants**; Inhibit bladder contractions, sedation and retention → overflow incontinence.
- **Psychotherapeutics**;
    - **Antidepressants**, **antiparkinsonian agents** and **antipsychotics**; Inhibit bladder contractions and retention → overflow incontinence.
    - **Sedatives** and **hypnotics**; Lead to sedation and impaired cognition → functional or overflow incontinence.

- **Others**;
  - **Alcohol**; Leads to diuretic effect and depressed central inhibition → urge incontinence, overflow incontinence or both.
  - **Antihistamines** and **anticholinergics**; Inhibit bladder contractions, sedation and retention → overflow incontinence.
  - **Medications for urinary urgency**; Inhibit bladder contractions, sedation and retention → overflow incontinence
  - **Thiazolidinediones**; Increase fluid retention → nocturnal diuresis and functional incontinence.

Diagnosis:-

- **History**; is *essential* to the **evaluation** of **urinary incontinence**.
- **Assess** *for* **transient incontinence**; *apply* **DIAPPERS mnemonic**.
- **Incontinence questions**;

1) During the past three months, have you leaked urine (even a small amount)?

☐ Yes ☐ No (questionnaire completed)

2) During the past three months, did you leak urine: (*check all that apply*)

☐ A. When you were performing some physical activity, such as coughing, sneezing, lifting, or exercising?

☐ B. When you had the urge or the feeling that you needed to empty your bladder, but you could not get to the toilet fast enough?

☐ C. Without physical activity and without a sense of urgency?

3) During the past three months, did you leak urine most often: (*check only one*)

☐ A. When you were performing some physical activity, such as coughing, sneezing, lifting, or exercising?

☐ B. When you had the urge or feeling that you needed to empty your bladder, but you could not get to the toilet fast enough?

☐ C. Without physical activity and without a sense of urgency?

☐ D. About equally as often with physical activity as with a sense of urgency?

- **Type of urinary incontinence are based on responses to question 3**;

Response to question 3	Type of incontinence
A. Most often with physical activity	Stress only or stress predominant
B. Most often with the urge to empty the bladder	Urge only or urge predominant
C. Without physical activity or sense of urgency	Other cause only or other cause predominant
D. About equally with physical activity and sense of urgency	Mixed

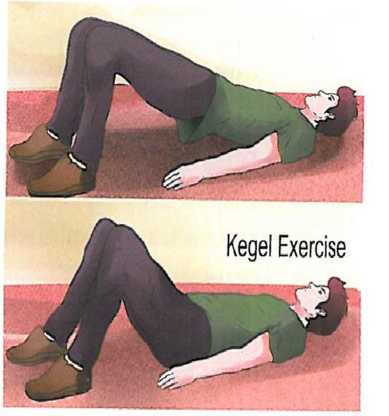
- **Assessment** *of* **quality of life**.
- **Voiding diary**; *can be helpful*;
  - **Stress incontinence**; usually wake once or not at all at night to void.
  - **Urge incontinence**; usually wake more than twice and as often as every hour.
- **Physical examination**; **Neurological**, **pelvic floor** and **musculoskeletal** ***examination*** can help for **medical conditions** *causing* **incontinence**.
- **Cough stress test**; patient **relaxes**, then **coughs** ***vigorously*** as the **doctor** *watches for* **loss** of **urine**.

Type	Cough stress test
Stress incontinence	Leakage coincides with coughing
Urge incontinence	May show delayed leakage after cough
Mixed incontinence	May show leakage with coughing
Overflow and Functional	No leakage

- **Urinalysis**; can help for; **infection**, **urinary stones**, or ***other*** **contributing causes**.
- **Post-void residual (PVR) urine**; - **Stress**, **Urge** and **Mixed incontinence**; < 50 mL.
  - **Overflow incontinence**; > 200 mL. - **Functional incontinence**; Varies

➢ **Managements:-**

Non-pharmacologic Therapy



- **Pelvic floor exercises** (**Kegel exercises**); are *first line* for **stress**, **urge**, or **mixed UI**.
- **Exercise** & **weight loss**; **patients** *with* **BMI >30**.
- **Bladder training** to *increase* **time** *between* **voiding** in **urge incontinence**.
- **Biofeedback** to *teach* **pelvic floor** *exercises*.
- **Scheduled** and **timed voiding**; may be *helpful for* **patients** *with* **dementia**.
- **Surgical repair** may be *helpful for* **stress incontinence**.
- **Pessaries**, **collagen**, or **bulking agent** *injections* also *help* **stress incontinence**.
- **Prostatectomy** in **men** or **self-catheterization** for *severe* **overflow incontinence**.
- *Several* **electrical neuromodulator devices** (Urgent® PC) are *approved by* **US FDA** for **urge incontinence** *refractory* to **behavioral strategies** (bladder & pelvic floor muscles exercises).

Pharmacological Therapy

Stress Incontinence

- ***No medications*** are **FDA-approved** for the *treatment of* **stress incontinence**.
- **α-adrenergic agonists**, such as **Pseudoephedrine** and **Phenylephrine**, cause **urethral constriction**.
- **Serotonin/norepinephrine reuptake inhibitor**; **Duloxetine**; has been shown to *reduce* **stress incontinence**.
- **Intravaginal Estrogen** therapy may have *several* ***positive*** **effects** in patients with **stress incontinence** who are **estrogen** ***deficient***. (**Systemic Estrogen** has been shown to ***worsen*** **incontinence**).

Urge Incontinence – Overactive bladder (OAB)

- **Anticholinergic Drugs**; **Oxybutynin**, **Tolterodine**, **Fesoterodine**, **Trospium**, **Solifenacin** and **Darifenacin**; They ***reduce*** **detrusor overactivity** by ***antagonizing*** **M_3 muscarinic receptors** in the **bladder**. ***Longer-acting formulations*** may be ***better*** **tolerated**.
- **β_3-Agonist**; **Mirabegron**; ***approved by*** the **FDA** in **2012**, **Mirabegron** act on **β_3-adrenergic receptors** to ***relax*** the **detrusor**. ***Common adverse effects*** are **nausea**, **diarrhea**, **constipation**, **dizziness**, and **headache**. ***Increased*** **blood pressure** ***can*** **also** *occur*, and **Mirabegron** ***should not*** be used in **patients** with ***uncontrolled*** **hypertension**.
- **Botulinum toxin A**; ***injection*** of into the **detrusor muscle** can ***prevents*** **stimulation** of **detrusor muscle** be and *using for* **urge incontinence** that has ***not responded*** to **conservative treatments**.
- **Intravaginal Estrogen** is *sometimes* ***used to*** treat **urge incontinence**.

Mixed Incontinence

- ***Focus on*** **symptoms** that ***dominate*** and ***consider*** **treatments** for **individual components** (**stress** or **urge**).

Overflow Incontinence (Urinary Retention)

- **Cholinomimetics**; **Bethanechol**; act by ***activating*** **muscarinic receptors** in the **bladder** and ***stimulating*** **contraction** to **void** the **urine**.
- **α_1-Receptor Antagonists**; **Prazosin**, **Doxazosin**, **Terazosin**, **Alfuzosin**, **Tamsulosin** and **Silodosin**; relax **prostate** and **urethra muscles** and ***relax*** **bladder neck**.
- **5-α-Reductase Inhibitors**; **Finasteride** and **Dutasteride**; *slow progression* (*prevent* prostate enlargement)
- **Phosphodiesterase-5 Inhibitors**; **Tadalafil**; **smooth muscle relaxation** in the **bladder**, **urethra** and **prostate**.

Functional Incontinence

- ***No drug treatments***. **Consider interventions** to ***remove*** *any* ***potential*** **cause**, **barriers** or **obstacles**; ***provide*** **schedules** or ***prompted*** **toileting**.

➢ Urinary Incontinence in Children:-

- **Types of Urinary Incontinence in Children**;
  - **Primary Enuresis**; is **wetting** in a **child** who has ***never been** consistently* **dry**.
  - **Secondary Enuresis**; is **wetting** that ***begins** after **at least*** **6 months** of **dryness**.
  - **Nocturnal** (**Nighttime**) **Enuresis**; is **wetting** that ***usually occurs** during* **sleep**.
  - **Diurnal** (**Daytime**) **Enuresis**; is **wetting *when* awake**.
- ***Prevalence***;
  - By **5 years** of **age**, ***more than* 90%** of **children** can ***control* urination *during*** the **day**.
  - **Nocturnal** (**Nighttime**) **Enuresis**; is ***more common*** than **daytime enuresis** in **children**, ***affecting*** **30%** of **4-year-olds**. The condition ***resolves* itself** (*about* 10% of 7-year-olds, 3% of 12-year-olds and 1% of 18-year-olds continue to experience nocturnal enuresis).

Nocturnal Enuresis (Bedwetting)

- **Causes**; *exact cause is not known*;
  - * **Slower Physical Development**; ***small* bladder capacity** (5-10 years old), ***long* sleeping periods**, and ***underdevelopment*** of the **body's alarms** that **signal** a ***full*** or ***emptying*** **bladder**.
  - * **Overproduction of Urine at Night**; The body *produces* **antidiuretic hormone** (**ADH**), a **hormone** that ***slows down*** the **production** of **urine**. ***More* ADH** is **produced** at **night** so the **need** to **urinate *lessens***.
  - * **Structural Problems**; *rarely*, ***blocked* bladder** or **urethra** (*bladder to overfill and leak*) and **nerve damage** (*spina bifida*).
  - * **Attention Deficit Hyperactivity Disorder** (**ADHD**); **Children** *with* **ADHD** are **3 times *more likely*** to have **bedwetting** than ***children without*** **ADHD**.
  - * **Obstructive Sleep Apnea** (**OSA**); ***Successful*** **treatment** of **OSA** often ***resolves* bedwetting**.
  - * **Genetics**; **Children** have a **30% chance** of *having* **bedwetting** if **one parent** was affected as a **child**.
- ***Managements***;
  - ***Non-Pharmacological Therapy***;
    - * **Fluids**; **Children *should be*** *instructed to* **drink** an **amount of fluids *during*** the **day**, and to **drink *enough*** to *prevent* **thirst** when they ***arrive* home** *from* **school** and at **bedtime** (***should be* restricted 2 hours *prior to*** **bed**).
    - * **Waiting**; **Urologists** and **paediatricians *frequently*** *recommend* ***delaying* treatment *until*** the **child** is ***at least*** **six** or **seven years old**.
    - * **Alarm Therapy**; is a **device** that **wakes** a **child** who **wets** the **bed** (*sensor clips to underpants*), ***in time***, the **child** is **wake** *when* the **bladder** is **full** (*before wetting begins*).
    - * **Alarm clock**; It may be **possible** to ***condition*** **older children** to **wake** to **void *by using*** an **alarm clock** (or **mobile phone alarm**).
  - ***Pharmacologic Therapy***;
    - * **Desmopressin**;
      - **Desmopressin** is a ***synthetic*** **replacement** for **antidiuretic hormone** (**ADH**) or **vasopressin**, the **hormone** that ***reduces* urine *production*** *during* **sleep**.
      - **Desmopressin** is the ***first-line treatment*** for **enuresis** in **children *older than*** **5 years**.
      - ***Dose***;
        - **Regular tablets**; 0.2 mg one hour before bedtime, if needed after 10 to 14 days, the dose may be increased by 0.2 mg to a maximum dose of 0.6 mg.
        - **Oral melt tablets**; 120 µg are given 30 to 60 minutes before bedtime; if needed after 10 to 14 days, the dose may be increased by 120 µg to a maximum dose of 360 µg.
    - * **Anticholinergic agents**;
      - ***Such as*** **Oxybutynin** in a dose of 2.5-5 mg administered at bedtime, may be used in ***combination with*** **Desmopressin** to ***increase* bladder capacity** *during* **sleep**.
    - * **Tricyclic Antidepressants**;
      - **Imipramine** is **used *most often*** in the ***treatment*** of **enuresis**; ***decrease*** the **amount of sleep**, ***relax*** the **detrusor muscle** (***anti-muscarinic***) and ***stimulate*** **vasopressin** secretion.